# PROSPECTIVE STUDY ON THE EFFECTIVENESS OF MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND THERAPY IN THE TREATMENT OF UTERINE FIBROIDS

*Dissertation submitted to*

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## CERTIFICATE

This is to certify that the dissertation entitled "**PROSPECTIVE STUDY ON THE EFFECTIVENESS OF MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND THERAPY IN THE TREATMENT OF UTERINE FIBROIDS"** is a bonafide work done by **Dr.A.DEVI LAKSHMI** in the Institute of Social Obstetrics, Govt Kasturba Gandhi hospital (Madras Medical College) Triplicane , Chennai, in partial fulfillment of the university rules and regulations for award of MD degree in Obstetrics and Gynecologyunder my guidance and supervision during the academic year2010-2013.

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## DECLARATION

I solemnly declare that this dissertation entitled **"PROSPECTIVE STUDY ON THE EFFECTIVENESS OF MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND THERAPY IN THE TREATMENT OF UTERINE FIBROIDS"** was done by me at The Institute of Social Obstetrics, Govt Kasturba Gandhi Hospital, Madras Medical College during 2010-2013 under the guidance and supervision of, **Prof. Dr. P.M. GOPINATHMD. DGO.** This dissertation is submitted to the TamilNadu Dr.M.G.R.MedicalUniversitytowardsthe partial fulfillment of requirements for the award of M.D Degree in Obstetrics and Gynecology (Branch-II).

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# CONTENTS



**s**

# INTRODUCTION

# INTRODUCTION:

Uterine fibroids mainly occur in 30 % of women over 30 years in their reproductive age causing severe personal, social and economic problems.[1] These fibroids are mostly asymptomatic, but women approach medical facilities with symptoms of menorrhagia, pain during cycles, pressure symptoms (increased frequency of micturition, constipation and nocturia), infertility and problems with pregnancy.[2]

Since many years the most common form of therapy for uterine leiomyomas has been hysterectomy and occasionally myomectomy. ***THE OPTION FOR WOMEN ALL THESE YEARS WAS STARK: EITHER TO SUFFER WITH THE INTENSE DISCOMFORT OR ENDURE MAJOR SURGERY.*** Of latest, many conservativeoptions instead of hysterectomy and myomectomy have been introduced.[3] Among them the most accepted and admired are hysteroscopic myomectomy and uterine artery embolization. These have certain limitations

regarding the size of the fibroids and the requirement for general anesthesia. (Fig1)

| | Procedure Time | Hospital Days | Return to Normal Activity | Adverse Events |
|---|---|---|---|---|
| Watchful Waiting | 0 | 0 | - | Fibroids can continue to grow, leading to worsening symptoms and the need for surgery |
| Drug Therapy | 0 | 0 | - | Effective for only 6-12 months; causes menopausal symptoms; may result in rapid return of symptoms when treatment is stopped |
| MRgFUS | 3 hours | 0 | 1 day | Skin burns, muscle pain |
| UAE | 0.75-2 hours | 1 night | 2 weeks | Post embolization syndrome, injury to a vessel or ovaries, blood clots, uterine infection |
| Myomectomy | 1-3 hours | 1-3 nights | 2-6 weeks | Post op. infection, wound infection, internal organ injury, possible c-section in future pregnancy |
| Hysterectomy | 1.5-3 hours | 2-5 nights | 4-6 weeks | Post op. infection, bleeding, injury to intestines, bladder, loss of reproductive potential |

Fig 1: Comparing the various choices of treatment for uterine leiomyomas by extent of invasiveness. [28]

Uterine artery embolization (UAE) has become a gold standard conventional interventional procedure for treating symptomatic fibroids.[12] However it has certain complications like pain after procedure and Post Embolization syndrome.[4] Minimally invasive percutaneous treatments using thermal ablation procedures have also been introduced. Treatment of uterine leiomyomas with radiofrequency ablation [13], cryoablation [14,15] , and laser therapies[16] have been reported.

Since many years, the interaction of ultrasound energy with body tissues has been utilized. As early as 1927, it was recognized that ultrasound energy could cause a rise in tissue temperature, and it was applied therapeutically rather than as a diagnostic modality.[5]

The energy level of ultrasound is very high such that when focused to a target tissue at a point it leads to protein denaturation and tissue necrosis with a temperature greater than $55^{o}$ C.[6]

Magnetic resonance guided high intensity focused ultrasound (MRgFUS ) therapy of fibroids is a proven technique approved by US Food and Drug administration for treatment of leiomyomas by heat generated using high intensity focused ultrasound.[4]

Benefits of MRgFUS are as follows: rapid relief from symptoms of uterine leiomyomas, speedy recoverytimes, very rare post-operative complications in comparisonwith UAE or hysterectomy, andvery rare occurrence of adverse effects.[17]

It can improve fibroid related symptoms and cause shrinkage of fibroids in due course of time. The aim of this study is to evaluate the clinical efficacy of this procedure in patients with symptomatic fibroids using clinical symptom severity scoring (SSS) before the procedure and after 6 to 12 months follow up.

# AIMS AND OBJECTIVES

**AIM OF THE STUDY:**

**TO STUDY THE EFFECTIVENESS OF MAGNETIC RESONANCE GUIDED HIGH INTENSITY FOCUSED ULTRASOUND IN THE TREATMENT OF SYMPTOMATIC UTERINE LEIOMYOMAS IN TERMS OF CLINICAL IMPROVEMENT.**

**OBJECTIVE:**

WHETHER MRgFUS CAN BE CONSIDERED AS A PRIMARY MODE OF NONINVASIVE TREATMENT OF UTERINE FIBROIDS.

**PRIMARY OUTCOME:**

- THE DEGREE OF SYMPTOM RELIEF AFTER THE PROCEDURE AT 6 MONTHS.
- THE IMPROVEMENT IN HEMATOCRIT.
- THE MEAN FIBROID SHRINKAGE AT 6 MONTHS AFTER THE PROCEDURE AND TO CORRELATE IT WITH THE IMMEDIATE NONPERFUSED VOLUME RATIO.
- ANY ADVERSE EFFECTS RELATED TO THE PROCEDURE.

**SECONDARY OUTCOME**:

- THE DEGREE OF SYMPTOM RELIEF AT 12 MONTHS.
- THE REQUIREMENT OF ANY ADDITIONAL PROCEDURE.

# REVIEW OF LITERATURE

## REVIEW OF LITERATURE:

1. **Lele** in 1975, described that ultrasound waves are suited for the tissues in depth because of their higher penetrating capacity through soft tissue than infrared and laser beams.[6]

"Focused ultrasound technology fulfillsprerequisites of aperfect surgical tool. It has the established capacity to damage the selected targets situated deep within tissue without affecting the tissue in the path or those around the lesions."

2. **Hynynen et al**. elaborated thesubstantial potential of this technology combination, andtheir theory was supported with results obtained from testing in animals.[26]

3. **Cline and Jolesz et al** in 1995..The authors concluded that with the guidance of Imaging ,defining target accuracy and control for thermal therapy in a variety of tissues with various rates of perfusion could be accomplished with precise thermal imaging feedback.[23]

4. **Hyun S. Kim,et al** concluded that long term results were acceptable because long term follow up of patients treated with HIFU showed good relief of symptoms which was sustained. [4].

5. **Jonathan Hindley et al** conducted a study on early results and concluded on follow up that symptomatic improvement was significant in 79.3% of patients who were treated. The average fibroid volume shrinkage at 6 months was 13.5%, but

non enhancing volume (mean, 51 cm3) remained within the treated fibroid at 6 months. [3]

6. **Summia Zaher et al** studied patient suitability for MRgFUS-moderationmethodspermitfor less restraining MRgFUS selection criteria for therapyfor symptomatic uterine leiomyomas and are anticipated to enlarge the pool of patients.

7. **Rabinovici et al**, concluded that earliest pregnancy experience after HIFU treatment has been promising, with an increased rateof delivered and continuing pregnancies. (Fertil Steril2010;93:199–209).

8. **Krzysztof R. Gorny,Elizabeth A. Stewart et al**. evaluated 12 month outcome and concluded that MR-guided focused US is an innovative noninvasive mode of therapy for uterine leiomyomas that can be used successfully and without any harm to treat uterine fibroids and brings about noteworthy sustained symptom relief that lasts at least for one year.

The incidence of additional procedures for persistent symptoms during the study was analogous to those in earlier studies of uterine artery embolization.

9. **Suzanne D. LeBlang** conducted a study to evaluate the amount of fibroid ablation and shrinkage after MRI-guided high intensity focused ultrasound therapy

and the outcomes revealed that the meanNonperfused volume ratio was 55% ± 25% soon after treatment with mean fibroid volume shrinkage of 31% ± 28%.[39]

11. **Taran et al.** organized and conducted a study comparing the most conventional treatment for uterine leiomyomas, hysterectomy and MRgFUS in a matched group of patients selected contemporaneously. The non-invasive, outpatient MRgFUS procedure was linked with very few adverse events both during and after the procedure in contrast with surgical hysterectomy. Similarly, patients treated with MRgFUS recovered faster and returned to work the next day, and the loss of work days was only one day for HIFU, whereas it was six weeks for hysterectomy. The symptomatic relief lasted longer in proportion to the percentage of ablation of the fibroid which corresponds to the Non Perfused Volume ratio.[34]

12. **Okada et al** confirmed in his study that the symptomatic outcome can be improved by ablating larger areas of the leiomyoma. They also proved that obtaining a greater NPV ratio is safe and to achieve the maximum treatment response, this must be the goal of treatment.[36]

13. **Funaki et al**. presented that the character of fibroids on MR imaging bears a great influence on the outcome. Fibroids with Low-intensity T2 signal respondsimmensely well, and hence larger areas of destruction are produced resulting in larger NPV ratios. On the contrary, T2 signal high intensity fibroids do not respond well and outcome is not achieved as desired.[44]

14. **Elizabeth A. Stewart, Amy K. O'Sullivan et al** studied regarding cost-effectiveness and their findings suggest that MRgFUS is in the range of presently acknowledged standards for cost-effectiveness, end to end with hysterectomy and uterine artery embolization.

15. Researchers who participated in the clinical trials condensed their opinion of MRgFUSas given below:

"Weconsider that MRgFUS therapy offers a potentially noteworthy novel noninvasive and valuable therapy for uterine leiomyomas, specifically in patients who request to keep away from invasive or agonizing therapies. The deprivation of invasiveness in MRI-guided focused ultrasoundtreatment rendersit remarkably fascinating and charismatic. We also emphasize that MRI-guided focused ultrasound treatment for leiomyomas might ascertain to be acrucial model for the expansion of this noninvasive, meticulous, well regulated and planned, tissue ablating technology to many other diseases".

# OVERVIEW

## OVERVIEW

## UTERINE LEIOMYOMA

Uterine leiomyomas are benign smooth muscle neoplasms that classically arise from the myometrium. They are frequently referred to as uterine fibroids and because their considerable collagen content creates a fibrous consistency, they are incorrectly called fibroids. Fibroids can be as small as a pea and can grow to become as large as a pregnancy at term.

Incidence is generally 20-25% in reproductive age group women. But has been shown to be as high as 70-80% as per histopathology or by ultrasoundexamination. In many women, fibroids are clinicallyimmaterial. On the contrary, their number, size or location within the uterus can provoke a variety of symptoms. Of all inpatient hospitalizations, fibroids comprise 27% of gynecologic admissions.

Fibroids are benign monoclonal tumors of the smooth muscle cells of the myometrium and comprise of larger clusters of extracellular matrix composed of collagen, elastin, fibronectin and proteoglycans.

## ETIOLOGY OF FIBROIDS:

**GENETICS**: They are monoclonal and about 40% have chromosomal abnormalities that include translocations between chromosome 12 and 14, deletions of chromosome 7, trisomy of chromosome 12.

**HORMONAL INFLUENCES**: Both estrogen and progesterone seem to favor the growth of fibroids. Fibroids are seldom detected before puberty and are most predominant among women of the reproductive age group, revert as they attainmenopause. Obesity and early menarche increase overall lifetime exposure to estrogen and increase the incidence. When estrogen exposure is less, as found with smoking, exercise and increase parity, it is protective. As a result of increased levels of aromatase activity within fibroids, de novo production of estradiol is higher than in normal myometrium. Fibroids have increased concentrations of progesterone receptors and thus progesterone is also important in the pathogenesis.

**GROWTH FACTORS**: Growth factors lie Transforming Growth Factor-β, Fibroblast growth factor increase smooth muscle proliferation. Vascular Endothelial Growth Factor promotes angiogenesis and stimulates synthesis of extracellular matrix. These factors are produced locally by smooth muscle cells and fibroblasts.

**RISK FACTORS:**

**AGE**: The incidence gradually increases with age. At 20 to 30 years, the incidence is only 0.31 per 1000 women years but by ages 45 to 50, incidence increases 20 fold to 6.2 per 1000 women years[19].

**Endogenous hormonal factors:**Greater exposure to estrogen as found with early menarche and late menopause decreases likelihood of having fibroids.

Polycysticovarian syndrome increases the exposure to estrogen and thus increases likelihood of fibroids[19].

**FAMILY HISTORY**: First degree relatives have 2.5 times increased riskof acquiring fibroids.

**ETHNICITY**: African American women have a 2.9 times greater risk of having fibroids than white women.

**WEIGHT**: Risk of fibroids increased 21% with each 10 kg increase in bodyweight.

**DIET**: Diet rich in beef, red meat increases the incidence. Diet rich in green vegetables decrease the risk.

**EXERCISE**: Women in highest category of physical activity (7 hours per week) are less likely to have fibroids.

**PARITY**: Increasing parity decreases the incidence of fibroids.The remodeling process of the postpartum myometrium including apoptosis and differentiation may be responsible for the involution of fibroids. Moreover vessels supplying fibroids regress during involution of uterus[20].

**SMOKING:** Nicotine inhibits aromatase and thus reduces conversion of androgens to estrogens.

**TISSUE INJURY**: Repetitive tissue injury to the endometrium and endothelium might promote the development of monoclonal smooth muscle proliferations in the muscular wall due to release of several growth factors.

**CLINICAL PRESENTATION**:

Fibroids are certainly not coupled with mortality but they might lead to morbidity and appreciably affect the quality of life. Most uterine myomas cause no symptoms. It is estimated that only 20 to 50% of women suffer from symptoms. The symptoms generally correlate with their location, number, size or concomitant degenerative changes[20]. They may present as follows:

- Asymptomatic
- Abnormal uterine bleeding-menorrhagia, anemia.
- Pelvic mass with pressure symptoms
- Urinary frequency, incontinence, hydronephrosis, constipation, tenesmus.
- Pelvic pain
- Reproductive dysfunction-Infertility.
- Pregnancy related-myoma growth, red degeneration and pain, spontaneous miscarriage.
- Malignancy very rarely.

***ABNORMAL BLEEDING***: About 46% of women with fibroids report gushing of blood during menstrual periods. Gushing of blood and duration of periods were correlated with the size of fibroids.

***PELVIC PAIN/DYSMENORRHEA***: Dysmenorrhea may be present when there is increased flow but pain as a symptom of fibroid is not frequent.

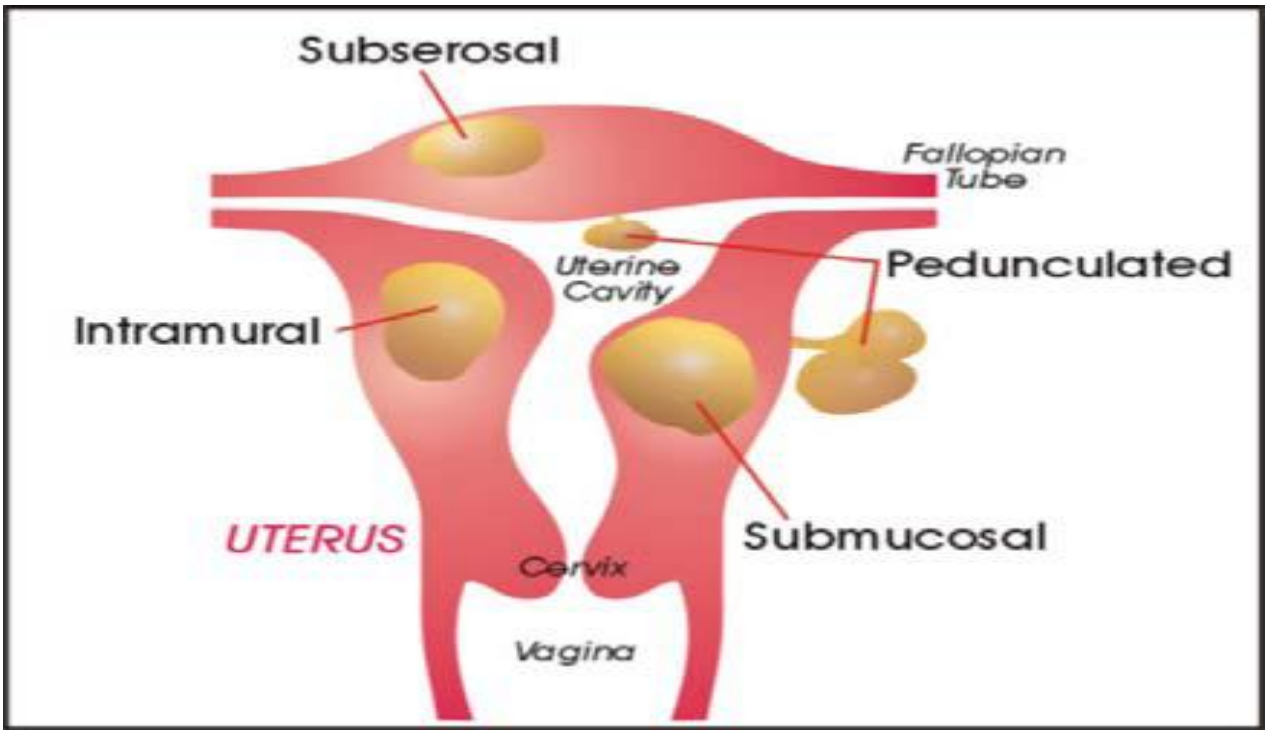
***PRESSURE SYMPTOMS***: As tumors grow pressure is exerted on the adjacent organs like urinary tract and recto sigmoid and thus symptoms like frequency, urgency, constipation, and tenesmus occur.

**DIAGNOSTIC IMAGING:**

***TRANSVAGINAL ULTRASOUND***: The efficacy is highly operator dependent and varies from 65 to 95%.The mapping accuracy decrease in larger uteri and with multiple fibroids.The addition of sonohysterography to TVUS greatly improves the sensitivity to 90%.

***MRI:*** The most accurate imaging modality for the diagnosis, mapping and characterization of leiomyomas.Nondegenerated fibroids appear with low signal intensity.

***FIGO FIBROID CLASSIFICATION[19]:***




**Sub mucosal**

- **0-intracavitary pedunculated**
- **1- <50% intramural**
- **2- >50% intramural**

**Others**

- **3-Abuts the endometrium without intracavitary component.**
- **4-Intramural and entirely within the myometrium without extension to either endometrial surface or to serosa.**
- **5-subserosal at least 50% intramural**

- **6-subserosal <50% intramural**
- **7-subserosal attached to serosa by a stalk.**
- **8-no involvement of myometrium, includes cervical lesions, those in the round or broad ligaments without direct attachment to uterus and parasitic fibroids.**

**MANAGEMENT:**

It is estimated that 25 to 40% of women in reproductive age group are affected by fibroids.The malignant potential of fibroids is <1% and thus the main aim of treatment is to provide relief of symptoms and improve quality of life, Small and asymptomatic fibroids don't need treatment and can be observed every 6 months.

***INDICATIONS FOR TREATMENT***[21]:

- Infertility caused by corneal fibroid blocking tubes, habitual abortion due to sub mucous fibroid.
- Fibroid more than 12 weeks size and a pedunculated fibroid.
- Asymptomatic fibroid causing pressure on the ureter leaving residual urine and infection.
- Rapidly growing fibroid in a menopausal woman.
- All symptomatic fibroids require treatment.

**TREATMENT MAY BE**:

- Watchful waiting.
- Conservative line of management.
- Definitive management.
- Recent advances.

***WATCHFUL WAITING***: Not having treatment seldom ends in any damage, apart from patients with severe fibroid related menorrhagia leading to anemia or hydronephrosis from ureteric obstruction due to a massively enlarged fibroid uterus. Thus, as women approach menopause watchful waiting may be considered, because there is limited time to develop new symptoms and after menopause bleeding stops and fibroids decrease in size[21].

***CONSERVATIVE LINE OF MANAGEMENT:***

Conservative line of management for fibroids includes

- Medical management and
- Minimally invasive surgeries.

***MEDICAL TREATMENT:***

Available options are

- LNG-IUS(MIRENA),
- GnRH Analogues
- RU-486

- Danazol

The above drugs have been used to treat fibroid associated menorrhagia and pain with limited success.

**Recent advances in medical therapy** include aromatase inhibitors like **Fadrazole**, Selective estrogen receptor modulators like **Raloxifene**, Selective progesterone receptor modulators namely **Asoprinil,Ulipristal acetate** have been introduced.

Mirena is useful only in small fibroids without distortion of cavity.

GnRH analogues are effective in shrinking fibroids and greatly improving menstrual symptoms but are limited by their side-effect profile especially osteoporosis and unpleasant menopausal symptoms. If given for 6 months, they reduce the fibroid volume by 30% and total uterine volume by 35%.They are only a short term solution for symptoms.

***Advantages of medical treatment[21]:***

- Avoids anesthesia and surgical risks.
- Cures menorrhagia, controlsanemia, cures pressure symptoms.
- Reduces the size of the tumor and blood supply, can be used preoperatively and allows use of laparoscopic myomectomy.

***DISADVANTAGES***:

- Side effects like hot flushes, vaginaldryness, transient frontal headache, arthralgia, decreasedlibido, and osteoporosis limit the duration of use.
- Failure of treatment.
- Recurrence of symptoms and regrowth after stoppage of treatment.
- Expulsion rates of LNG-IUS are higher in women with fibroids.
- Surgery may still be required.

***MINIMALLY INVASIVE PROCEDURES***:

*LAPAROSCOPIC GUIDED MYOLYSIS AND CRYOMYOLYSIS*[19]: A number of energy sources using bipolar electrosurgery, Nd: YAG laser and cryogenic probes were used under laparoscopic direction to reduce fibroid size by means of fibroid destruction and interference with local vascular supply.

*Advantages:*

- Ease and rapidity of surgery.
- Good hemostasis.
- Rapid recovery.

*Disadvantages*:

- Delay in reduction of uterine size
- Great risk for recurrence.

## DEFINITIVE LINE OF MANAGEMENT:

The definite line of management for fibroids traditionally include various surgical procedures viz, myomectomy and hysterectomy. In recent years myomectomy is being done through minimally invasive techniques like laparoscopic and hysteroscopic myomectomy.

### *MYOMECTOMY:*

Myomectomy should be considered a safe alternative to hysterectomy. VICTOR BONNEY stated in 1931 that "*THE RESTORATION AND MAINTENANCE OF PHYSIOLOGIC FUNCTION SHOULD BE THE ULTIMATE GOAL OF SURGICAL TREATMENT."*

Myomectomy whilst aiming to preserve fertility is also associated with morbidity and hospital stay and carries the risk of proceeding to emergency hysterectomy[21]. In addition it may also compromise reproductive potential and provide difficulties in long term management owing to high recurrence rate of fibroids and adhesion formation. Withmyomectomies, operating times were longer. Use of tourniquets, vasoconstrictiveagents, cell savers may be considered to limit the blood loss during myomectomy.

### *ADVANTAGES:*

- Removes fibroids and cures symptoms in one sitting.
- Improves fertility in 40% cases.

- Risk of malignancy eliminated.

***DISADVANTAGES:***

- Risks of anesthesia and surgery.
- Postoperative adhesions.
- Recurrence of fibroids due to growth of seedling fibroids.
- Persistence of menorrhagia in 5 to 10% due to congestion enlarged uterine cavity.

***HYSTEROSCOPIC MYOMECTOMY***:

In recent years, hysteroscopic myomectomy being minimally invasive is gaining popularity.Hysteroscopic myomectomy has become possible in a sub mucous fibroid.

***Advantages:***

- Minimally invasive.
- Lack of incision on the exterior of the uterus.
- Reduces likelihood of pelvic adhesions.

***Disadvantages:***

- Inadvertent perforation of uterus.
- Bleeding
- Intracavitary adhesions.

- Hyponatremia, hyperammonemia and cerebral edema can occur with use of electrolyte poor solutions.

***LAPAROSCOPIC MYOMECTOMY***:

Laparoscopic myomectomy is feasible in:

- A pedunculated fibroid.
- Subserous fibroid not exceeding 10 cm in size and not exceeding 4 in number.

Fibroid is retrieved through posterior colpotomy,minilaparotomy or morcellation.

Laparoscopic myomectomy was associated with longer operating times, reduced postoperative anemia. Reduced postoperative pain and speedy recovery of patients.

***Disadvantages***:

- Increased chance of bleeding due to nonapplicability of hemostatic clamp.
- Increased postoperative adhesions.
- Recurrence due to unrecognized small fibroid.

***SURGICAL HYSTERECTOMY:***

The traditional treatment of symptomatic fibroids is surgical, namely hysterectomy and myomectomy, But in recent times, if hysterectomy is offered as the first and only treatment option some women choose to accommodate to symptoms and stop seeking treatment. Hysterectomy ensures complete resolution of all symptoms and

is associated with a high patient satisfaction rate. However it is also associated with significant morbidity, relatively long hospital stay and guarantees infertility.

***Complications of hysterectomy***:

- Hemorrhage.
- Anesthetic complications
- Trauma to bladder, ureter, bowel during surgery.
- Wound infection.
- Abdominal adhesions.
- Thrombosis, pulmonary embolism.

***SEQUELAE OF HYSTERECTOMY***: In general women who had hysterectomies have significantly worse scores on quality of life questionnaires than women diagnosed with hypertension, heart disease and arthritis.

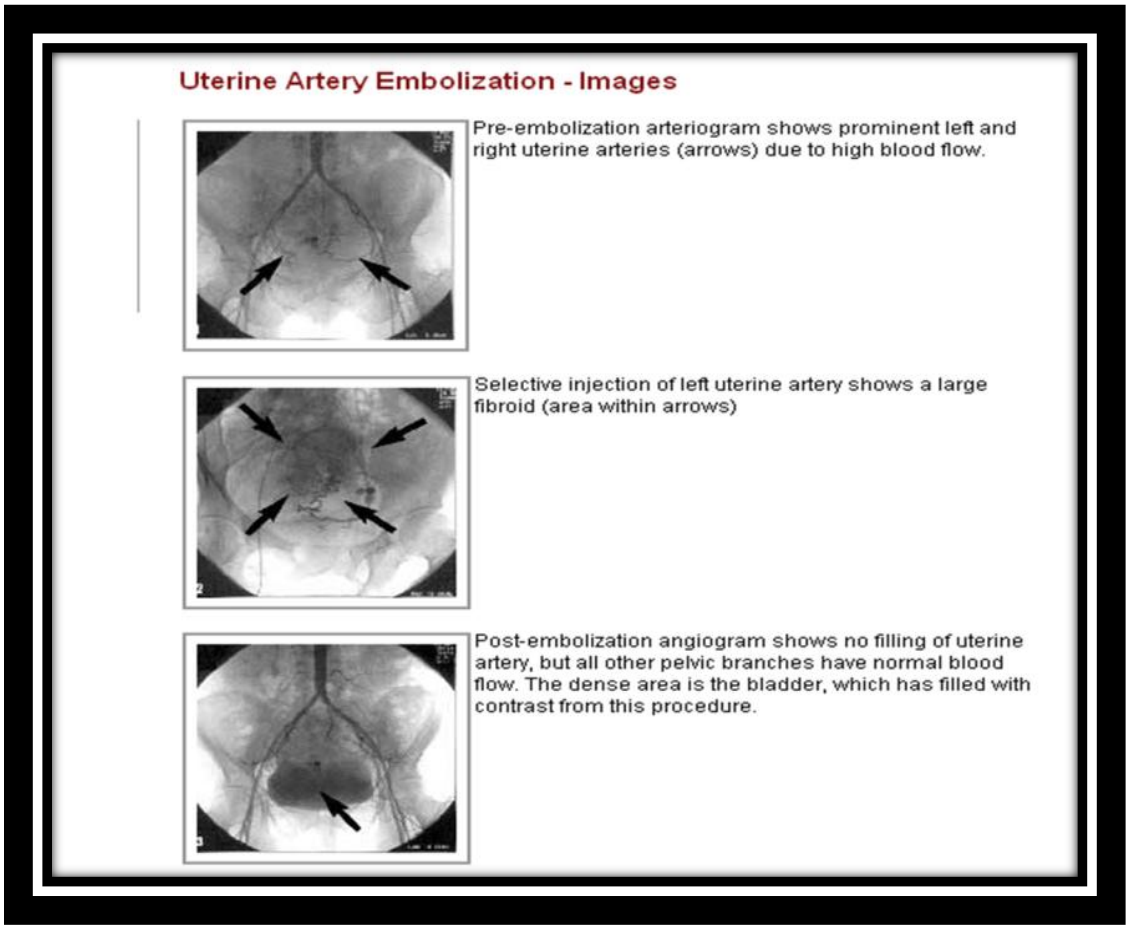
- Dyspareunia due to short vagina and ovarian adhesions to the vault.
- Chronic pelvic pain due to adhesions.
- Residual ovarian syndrome and ovarian cancer in 1% of left behind ovary.
- Vault prolapse.
- Granulation tissue at the vault requiring treatment.

## RECENT ADVANCES IN THE TREATMENT OF FIBROIDS:

***UTERINE ARTERY LIGATION***: Recently the surgical ligation of uterine arteries has been performed and evaluated.46% decrease in fibroid volume has been observed and symptomatic improvement was noted.

***UTERINE ARTERY EMBOLISATION***:

In 1991, Ravina first performed uterine artery embolization. The goal is to deliver particulate material-typically polyvinyl alcohol particles into both arteries to produce ischemic changes to myoma without causing permanent damage to the uterus.



***Contraindications*:**

- Subserous and pedunculated fibroids
- Sub mucous fibroid.
- Infertility and desire of pregnancy.

***Advantages:***

- ✓ No major surgery.
- ✓ No intraoperative bleeding.
- ✓ Short hospital stay.

***Disadvantages:***

- × Fever and infection.
- × Vaginal discharge and bleeding.
- × Ischemic pain suggests successful therapy but can be unbearable.
- × Pulmonary embolism.
- × Ovarian failure following accidental ovarian vessel blockage.
- × Fertility rate is reduced due to adhesions.

**MAGNETIC RESONANCE GUIDED FOCUSSED ULTRASOUND THERAPY:**

With the evolution of minimally invasive surgical and nonsurgical techniques and changing attitudes towards uterine preservation, the popularity of conservative

treatment options has escalated over the last decade. The noninvasive nature of MRgFUS holds particular attraction to women who intend to preserve the uterus.

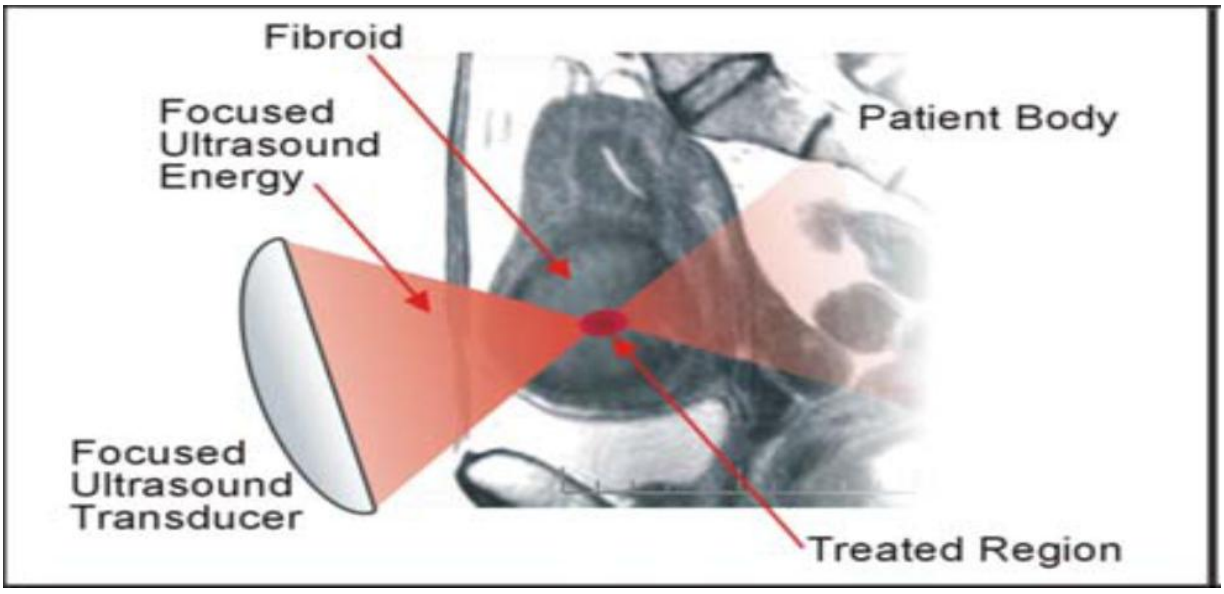
Though ultrasound imaging is classicallyrecognized as a diagnostic device, it was initially applied as a therapeutic rather than a diagnostic model. The use of ultrasound for medical ablative treatments has been recognized since 1920s.But limitations in accuracy and temperature monitoring hampered clinical development of this technique.

**PRINCIPLES:**

The principles of thermal ablation are that the application of heat leads to a localized tissue destruction. Since the resulting cell necrosis is a coagulative rather than ischemic necrosis, the painful infarction syndrome which is recognized after uterine artery embolization is avoided. In 2004, the U.S. Food and Drug Administration (FDA) approved the use of Focused ultrasound under Magnetic resonance guidance in the cure of uterine leiomyomas.[43] The feasibility of an MRI guided system was first described in 1995. Ultrasound waves of high intensity can be focused into a minimum volume of tissue to create an increase intemperature adequate enough to cause cell necrosis to the target that is deep in the body**.**

**"Imagine using a magnifying glass to focus the sun's rays on a single point to create a flame to burn a leaf"**.Just like that pulses ofenergy are repeated forentire

volume of fibroid.




Thus MRgFUS is a completely NONINVASIVE low risk therapy for treating uterine fibroids. It's like '**TAKING CORE OF AN APPLE WITHOUT CUTTING IT OPEN.'**

***CONCURRENT MR IMAGING ALLOWS***:

- 3-D anatomical information for exact tumor targeting.
- To visualize the entire beam path such that the treatment would be safe.
- To apply real time temperature monitoring to accomplish an outcome as intended.
- Post treatment contrast imaging to evaluate the effectiveness of the therapy.

The significant disparity between FUS and other forms of energy like radiotherapy is that the passage of ultrasound energy through intervening tissue has no apparent cumulative effect on that tissue.

The thermoablative element of MRgFUS ensues when numerous sound waves arising from an ultrasound source move across thedesired tissue andcongregate at a focal point in the target. Each individual burst of FUS energy is termed a sonication. Heating the tissue to more than 70 $^{o}$C will lead to tissue damage by inducing coagulative necrosis.[45] Tissue destruction is effectively accomplished through heat and cavitation effects by mounting up energy of high intensities in minimal volume of target tissue.

Normally ultrasound energy passes throughwithout causing any harm to the interveningtissue. This is because very minimal amounts of energy are absorbed and this absorbed energy is usually dissipated by the cooling effects of perfusion and conduction. If, conversely, the ultrasound waves carry an excessive level of energy and areconverged to a tight focus, an increase in temperature would be observed, since the energy conveyed by the beam would be swiftly converted into heat.

By rising the temperature to greater than 55 degree Celsius at the target point, the ultrasound waves can produce protein denaturation and thus end up in cell death. The resultant lesion of coagulative necrosis would be cigar shaped [3].

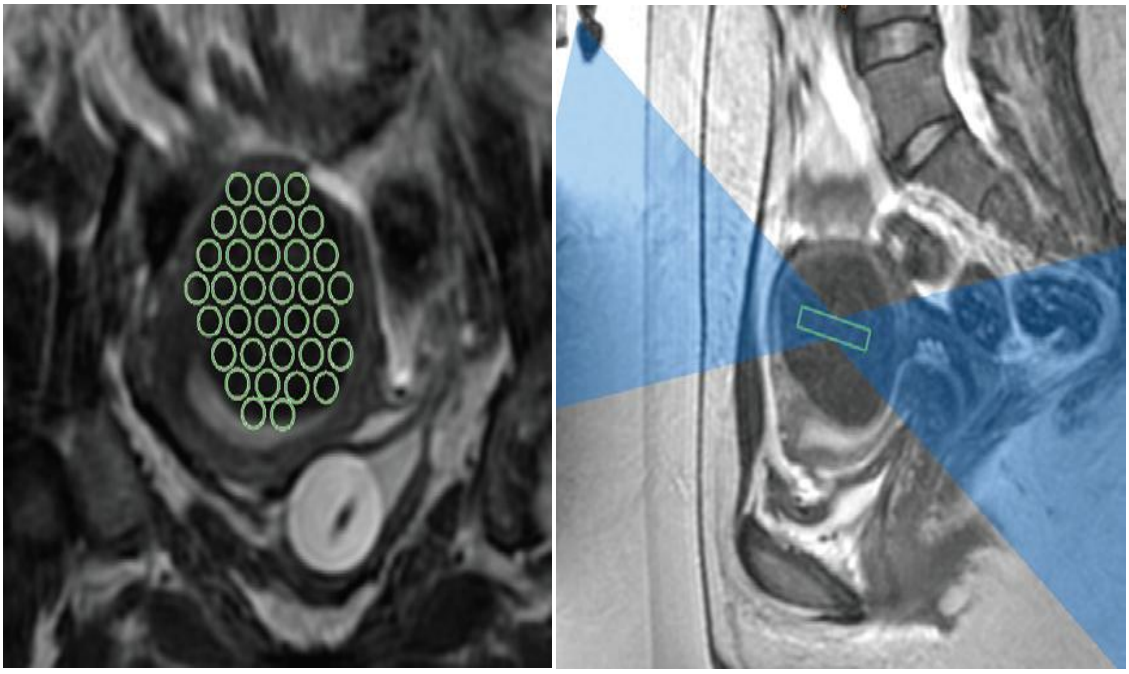
Theother surrounding tissues and the tissues through which the ultrasound beam crosses other than the target focus ,are just warmed but are not heated upto lethal temperatures and are thus not damaged even minimally.

As the temperature rises, there occurs a shift in proton resonant frequency and this can be recognized with the use of phase imaging[46]. When successive phase-shiftMR images acquired during each ultrasound sonication are evaluated and compared with the image taken just prior to that sonication, a real time thermal mapping of the rising temperature at the target and in the tissues surrounding the target can be generated by calibrating the changes in the recent images [47].

The MRI-guided focused ultrasound therapy system utilized assimilates completely with a 1.5-T MRI system such that the focused ultrasound therapy applied can be programmed instantly with the MR images and real-time MR thermometry feedback of every sonication can be obtained.

The ultrasound waves are generated from a piezoelectric plate contained within the transducer. Depending upon the size, shape and frequency of the ultrasound source, the generating ultrasound field is altered.[2] .Focusing of the ultrasound waves, can be done using lenses or reflectors, or by converting the transducer into a self-focusing one.

**TREATMENT PLANNING** **TREATMENT**



There is a computer-controlled positioning system, an amplifier system, and a user interface that are integrated with a MR imaging system (standard is 1.5 T). The lateral position and angle of the transducer can be mechanically controlled, and with beam steering the focusing depth and size of target focus can be controlled. [4]With this equipment ultrasound waves of high-intensity can be converged to a very minimal focal volume of tissue. The volume of destruction through ablation after each sonication pulse is very small, that is around 6 mm to 25 mm, and so numerous successive sonications are needed to create the desired effect.

Large temperature elevations and persistence of this high temperature for a sufficient period is necessary to create tissue damage[44]. The exposure of the target

point to this high temperature must exceed beyond a threshold time for optimal thermal damage. The tissue might recover when either of these does not exceed the threshold. Desired necrosis would occur when the heating results in a temperature more than 50 $^{o}$C and the same lasts for 10 seconds. Raising the temperature to higher degrees reduces the time required for necrosis.

Thus a temperature of 56 $^{o}$C would need only 1 second for necrosis and elevating the temperature to 60 $^{o}$C reduces the time for necrosis to 0.1 second. On the contrary, a temperature of 45 $^{o}$C will need a longer time as 1000 seconds to result in necrosis. Henceforth the desired result of coagulation necrosis can be obtained when the heating is increased to the appropriate temperature and is sustained for the threshold time, by producing protein denaturation and cell death. However, the tissues other than the focus which lie in the path of the ultrasound beam, are just warmed, only to temperatures that are sublethal.Achieving the optimal temperature elevation is influenced by many factors,viz,the type of tissue, the size, shape of the ultrasound beam, the presence of high vascularity which act as a heat sink[44].

The other effect caused by focused ultrasound is an acoustic cavitation effect[44]. In this effect, acoustic energy is concentrated in small gas bubbles that are generated by the energy from the ultrasound. This results in a substantial increase in the

absorption of ultrasound energy in tissue. Major tissue destruction might occur due to violent bubble collapse leading to significant energy release in the vicinity.

Enhancing the area of ablated volume during each sonication can be achieved through controlled micro bubble formation[49]. Thus with each sonication the resultant Nonperfused volume obtained would be higher.

**MRI Temperature Measurement Principles**:.

MRI has tremendous soft-tissue contrast and the capacity to generate immediate, quantitative temperature imaging in a range of tissues[46,47]. Temperature measurement in MRI can be done with an array of techniques: apparentdiffusion constant of water, the spin-lattice relaxation time, and the water proton resonance frequency shift (PRF). In response to changes in temperature,the proton resonance frequency of water changes.

The images are used to construct the temperature images acquired during the sonications. They are compared with a reference image obtained just prior to the sonications to create a real-time thermal map. Thus it helps us to monitor the temperature changes in the area of region of treatment.

**BENEFITS:**

The major benefits to the society are:

- Uterus sparing Noninvasive therapy for Fibroids

- Fast Outpatient Procedure
- High patient compliance
- Short recovery time. Return to normal activity in 1 to 2 days. No loss of work days.
- Safe and effective procedure, very rare complications.
- No Anaesthesia,No radiation, Noscars, No hospital stay
- Outpatient procedure – WALK-IN AND WALK-OUT PROCEDURE, no hospital stay.

Thus MRgFUS therapy provides a potentially new noninvasive and effective treatment of fibroids.The total lack of invasiveness and the fact that it is performed as an outpatient procedure makes it very attractive for patients.

MRgFUS offered women sustained relief from uterine fibroid symptoms for upto two years, with a low incidence of side effects, according to a study published in the August 2007 issue of Obstetrics and Gynecology. The 359-patient Mayo Clinic-led collaborative study also showed that destroying as much of the fibroid as possible leads to the most durable symptom relief with85% of the participants experiencing symptom improvement after one year.

**FUTURE DIRECTIONS OF MRgFUS:**

- Large leiomyomas are difficult to treat with MRgFUS primarily because of the longer duration to complete the procedure.To solve this problem, we can pretreat the fibroids with GnRH agonists. Treatment for 6 months reduces the myoma volume by 30%[52].
- Desire for future fertility:If MRgFUS is able to decrease the size of the fibroid and allow for a more normal endometrial cavity, itis possible that fertility may be improved[53]. Since manypatients with large fibroids or multiple fibroids require an abdominal myomectomy, this noninvasive procedure should be the first option. An on-going trial is underway forpatients with symptomatic uterine fibroids who desire pregnancy after undergoing MRgFUS treatment.[39]
- Other applications: There are studies investigating the use of MRgFUS in adenomyosis, breastcancer, prostatecancer, braintumours and in drug delivery systems.

# MATERIALS AND METHODS

## MATERIALS AND METHODS:

### PLACE OF STUDY:

The study was conducted in the Institute of Social Obstetrics, Govt Kasturba Gandhi hospital Chennai in collaboration with theDepartment of Radiology and Imaging, Bharat Scans, between January 2012 and December 2012 over a period of 12 months.

### TYPE OF STUDY:

Prospective study. The study was submitted to the scientific and ethical committee and was approved.

### INCLUSION CRITERIA:

Patients who presented with symptomatic fibroids[49] more than 18 years of age and who would have alternatively been offered traditional semi invasive or surgical treatment were selected for MRI guided focused ultrasound therapy.

### EXCLUSION CRITERIA:

1. Women with asymptomatic fibroids
2. Patients who were unsuitable for MRI. (Cardiac pacemakers,vascular clips etc.,)
3. Patients with serious systemic diseases.
4. Patients who weigh more than 150 kgs.

5. Fibroids more than 10 cm.
6. Patients with pedunculated fibroids with a slender stalk.
7. Patients who were pregnant during the procedure.
8. Patients with unmanageable bowel interposition and scars.
9. Deep seated fibroids. (> 13 cm from the anterior abdominal wall).
10. Fibroids with dense calcifications.

**METHODS OF ENROLLMENT:**

All patients who visited the Gynaec.O.P.Department at our institute were screened to verify who met the eligibility criteria[49]. They were sorted out and were thoroughly counseled regarding the procedure, the adverse effects that can occur during and after the procedure and after getting proper informed consent, they were included in the study.

The next step was to screen them for MR compatibility like excluding cardiac pacemaker, metallic implants and severe claustrophobia. The patient must be able to lie prone for about 3 hours and must be able to communicate sensations during the procedure. Importance was given to scars in the abdomen, as they may disrupt the passage of US waves. In our study, all suitable subjects were given questionnaires for symptom severity scoring which were assigned a score on a 4 point scale. No symptoms-score 0, Mild symptoms-score 1, moderate symptoms-

score 2, severe symptoms-score 3.These are subjective measurements for evaluation and monitoring.

**PREPROCEDURE MRI:**

All patientsunderwent a screening MRI of the pelvic region to assess the anatomic suitability of the therapy.T1W and T2W images were obtained in axial, coronal and sagittal planes. Skin surface was included in the coronal plane to assess the position of scars intervening the beam pathway. It was done with patients in prone position so that images obtained mat resemble as those of treatment.

The purpose of this screening MRI was:

- To confirm the diagnosis.
- To exclude associated adenomyosis, adnexal mass.
- To assess the exact number of fibroids, size, location and enhancement characters.

Small fibroids <3cm and large fibroids >10 cm were excluded due to the lack of ability to focus them or attain ideal necrosis.

***Other Parameters to be assessed in MR imaging***:

- The path of Ultrasound beam: If fibroid was >12cm from the anterior abdominal wall, US waves may not penetrate the target. If it is very close to the sacrum, increasing the temperature of the sacral bone might end up with sciatic nerve injury. Sonications must be limited to at least 4cm from the sacral bone. Allinterposing or contiguous organs in the path of treatment as well as scars must be avoided.
- Character of fibroids: There are two classes of fibroids[45].Classical fibroids are those with low signal on all pulse sequences and enhance homogenously.Hypercellular ones are those with high signal, highly vascularized and are difficult to treat and they have a poor outcome.
- Ideal patient is one with

  Anterior fibroid with uniform to low signal intensity, no intervening organ in pathway and with good perfusion.

**MRgFUS PROCEDURE**:

The MRI-guided focused ultrasound therapy systems used in this study PHILLIPS Sonalleve MR HIFU integrates with Achieva 1.5 T MR system to enable focused ultrasound therapy to be planned directly with MR images and to give real-time MR thermometry imaging after each sonication.

**PREPROCEDURE PREPARATION**:

- Patients were instructed to fast at least for 6 hours before the procedure. Ideal would be fasting for 12 hours.
- Abdomen was cleaned well and shaved from the xiphy sternum to one cm below the pubic bone to avoid any air bubbles trapped in hair which may increase the risk of burns.
- Conscious sedation with midazolam was given to alleviate anxiety and pain such that the patient was responsive throughout.
- Informed oral and written consent was obtained from all the participants after proper counseling about the procedure.
- Continuous bladder drainage was kept to keep the bladder empty because filling of the bladder during the procedure may dislodge the uterus and alter the location of leiomyomas.
- Patient was given a PANIC BUTTON during treatment such that she can stop the treatment when she has severe pain or heat sensation.

**TREATMENT PLANNING**:

Patient was made to lie down in prone position such that her abdomen was in contact with acoustic gel pad in a water bath of degassed and deionized water. Prior to initiating the procedure multilane $T_2$Wimages were taken and transferred for planning workstation. Region of treatment (ROT) was manually drawn and outlined confiningwithin the capsule of the fibroid.

Treatment areas were selected as small cells (Fig 2) of varying sizes ranging from 4mm to 32mm. Each cell was checked for safety in near field and far field. The cells were arranged in different clusters to cover the treatment area. (Fig 3)

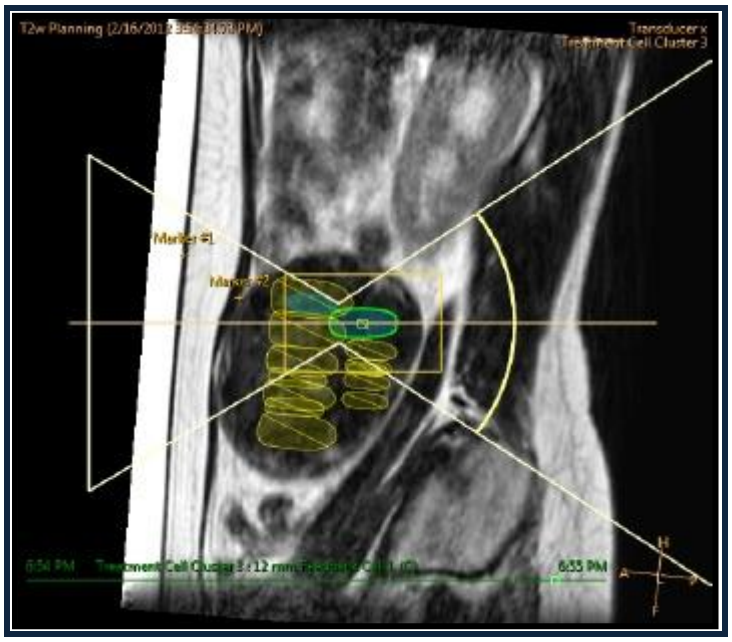



**FIG 2.** IMAGE SHOWS SAGITTAL SECTION IN PLANNING PHASE WHERE CELLS ARE ARRANGED IN THE TREATMENT AREA AND THE TRANSDUCER OVERLAY CAN BE SEEN AS ANGLED BEAM.

Target volume was analyzed with superimposed US beam paths in 3 planes. The beam path must be angled for optimal access of the fibroid such that scars, air bubbles and other intervening organs are avoided. If fibroid was close to the serosal surface, a 0.5cm margin of no targeted tissue should be maintained to prevent thermal damage to tissues in close proximity.

**TEMPERATURE IMAGING**:

Source of signal in MR are the chemical environment and relaxation properties of nuclei. It is sensitive to tumbling of molecules and thus sensitive to temperature. There are three parameters for thermal imaging, of which the most appropriate is the shift in proton resonance frequency which yields quantitative temperature monitoring. Proton resonance frequency has linear relationship with changes in temperature. Except for adipose tissue, it is tissue independent and is not affected by tissue coagulation.Thermal images were obtained during every sonication in all three planes with phase subtraction fast gradient echo proton resonance frequency-shift- dependent techniques[46].

**PROCEDURE:**

After thermal imaging and marking the region of treatment, the procedure was initiated with delivery of subtherapeutic doses of low power sonication (50-100W) to the center of fibroid[54]. Real time thermometry was acquired through proton

resonance frequency shiftmethod. The consequential images were offered for sonication location, to reassure the precision and accuracy of targeting.

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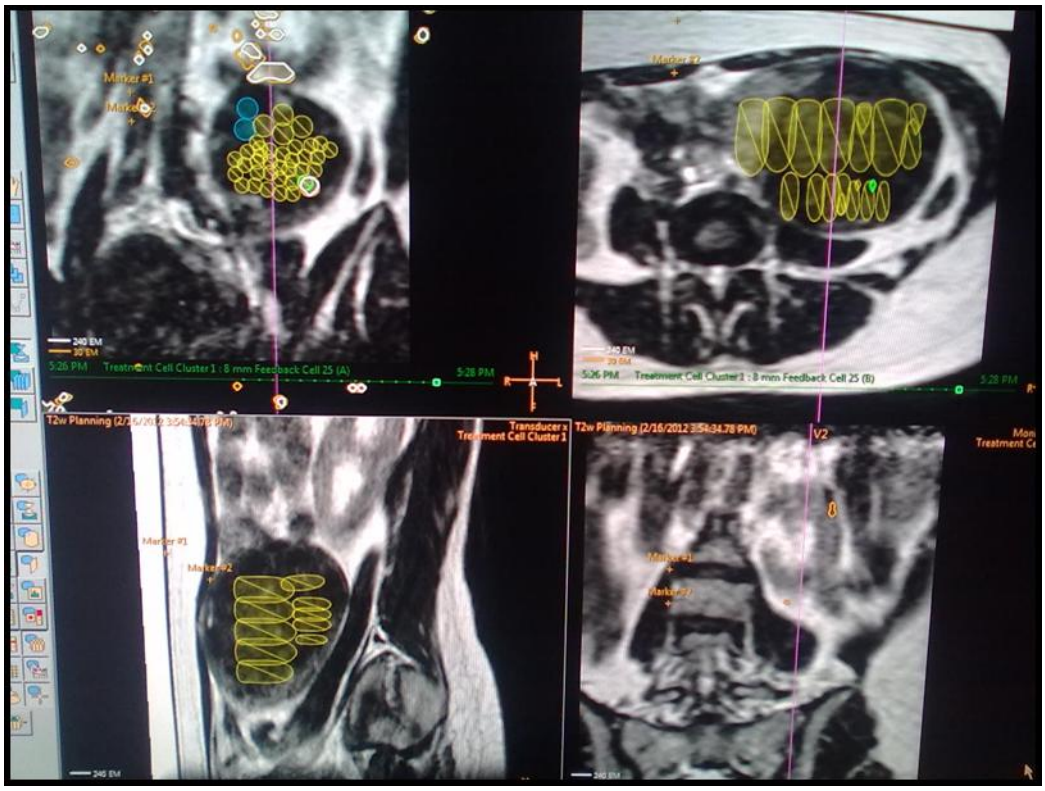


IMAGE SHOWS THE PLANNING SEQUENCE IN ALL PLANES.THE TREATMENT CELLS APPEAR CIRCULAR PERPENDICULAR TO THE BEAM AND THEY ARE “CIGAR SHAPED” PARALLEL TO THE BEAM.

A pre sonication image obtained was used as baseline and further images were added sequentially in a single sonication. Colorcoding (Blue to red scale) (Fig 4)

representing the gradual increase in temperature were projected over the treatment area. Special graph showing the temperature rise was also made available on the screen. Next sonication was done after the lapse of reasonable cooling time. The sonication parameters were safely adjusted using the thermometry graphs for further safe sonications.

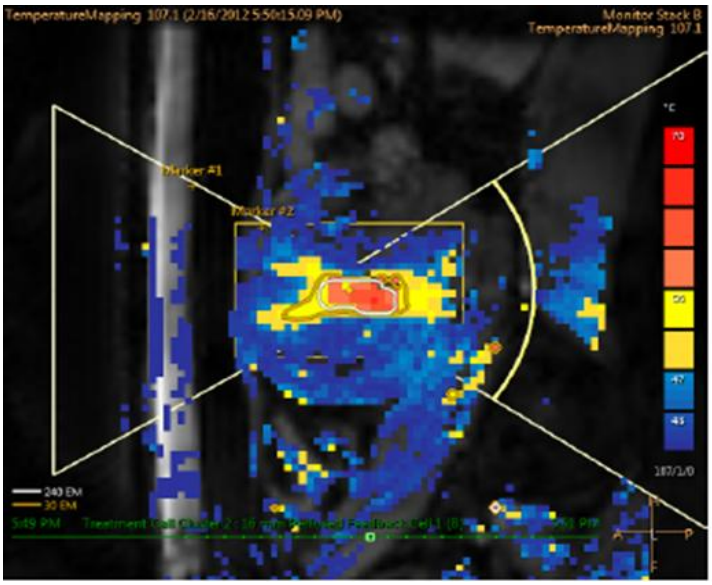



***Fig 4.*** *TEMPERATURE MAPPING SEEN AS COLOR CODES FROM BLUE TO RED.*

Subsequent sonications were given at therapeutic power level. Until therapeutic thermal dose, energy delivered was increased to coagulate the tissue at temperatures above $60^{o}$ C.It is desirable to try and reach 70-$80^{o}$C that ensures tissue necrosis. Each sonication lasts for 20-40seconds.Between each sonication sufficient cooling time should be given of upto 90seconds to avoid thermal buildup which will damage the surrounding tissues.

For all planned sonications the same procedure was continued. To be sure of no complications,constant interactionwith the patient wasimperative. The whole procedure would last for 3-4 hours.

*Criteria to terminate early were*:

- Failure to visualize focal treatment spot.
- When the patient complaints of unbearable pain.
- Targeting difficulties due to patient motion.

After completing all the planned sonications, the last step was to assess the NONPERFUSED VOLUME by giving intravenous gadolinium as contrast.

**POSTPROCEDURE:**

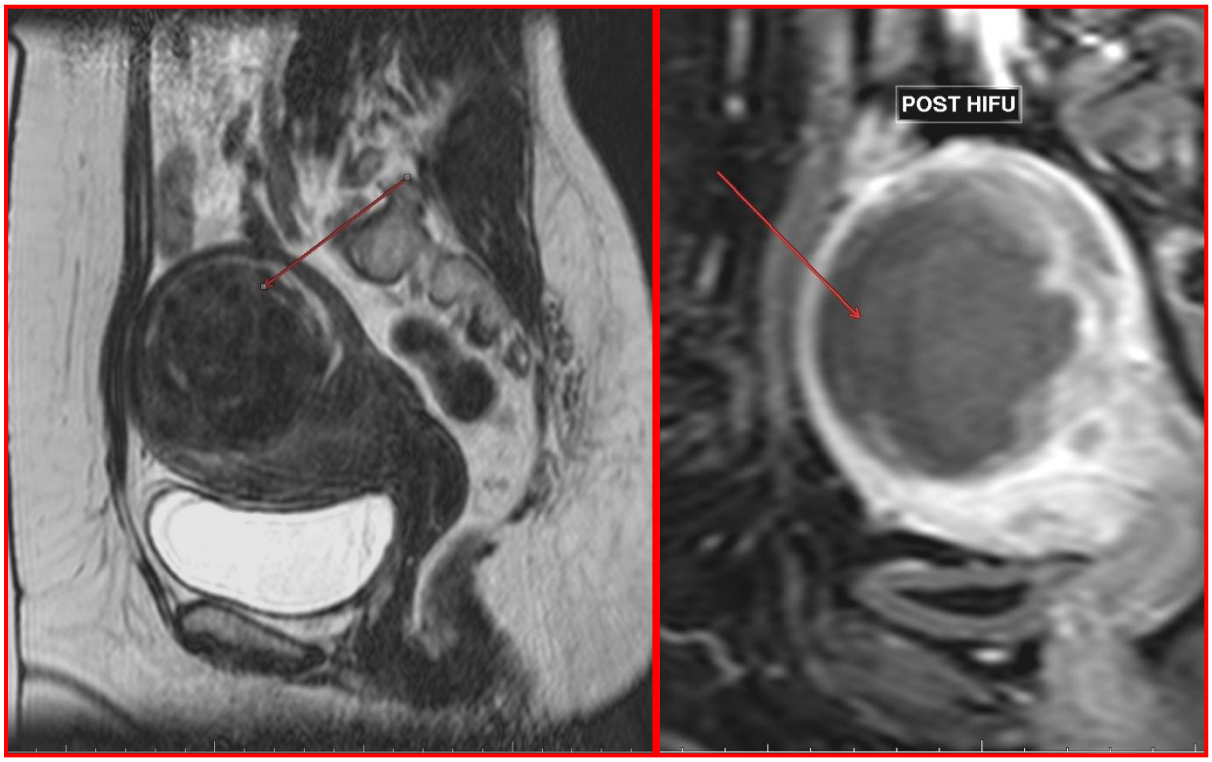
Following the procedure, the patient was taken to a holding area where the Foley's catheter was removed. The skin surface would be examined for any heat induced changes. Body temperature would be recorded. Patient would be instructed not to drive and to take rest till she recovers from the sedation. She can resume activities the following day. The most common symptom was mild back pain, fever and general discomfort. Patient was discharged after one to two hours observation after the procedure.

**FOLLOW UP OF PATIENTS**:

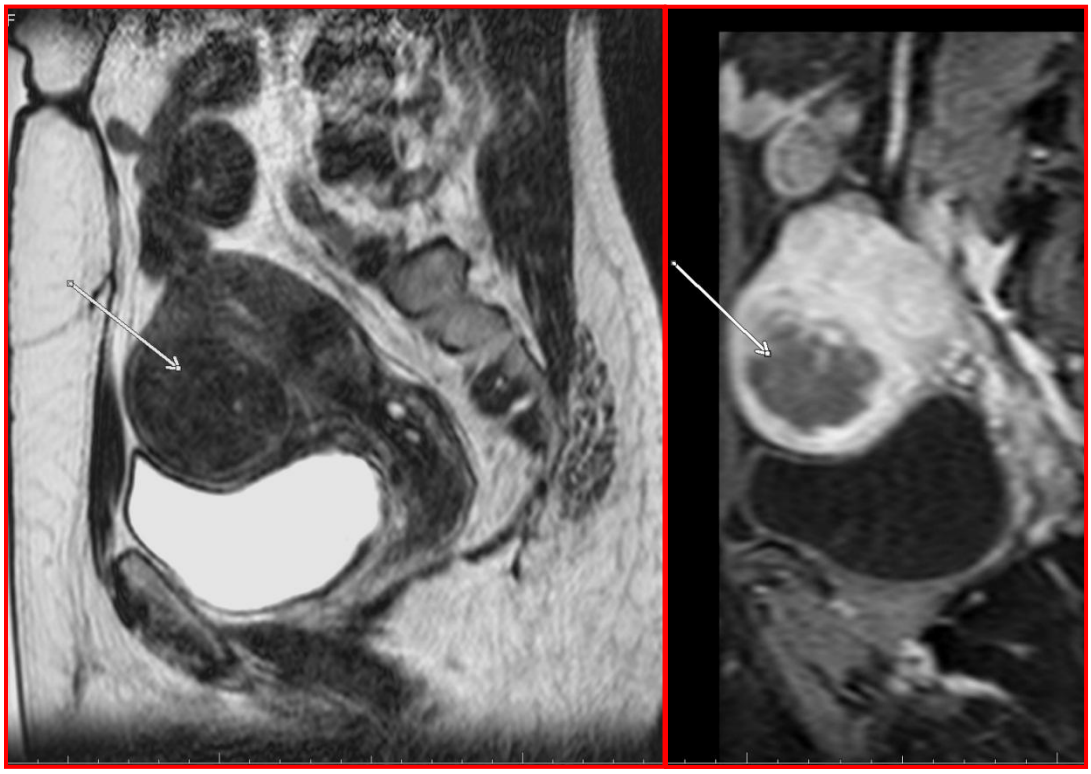
Patients were asked to come for follow up after 6 months and 12 months. They were given the same questionnaires regarding the improvement of symptoms. Their Hematocrit was measured and the values were noted. The fibroid shrinkage was assessed by clinical examination and Ultrasound pelvis.

**REPRESENTATIVE CASES:**

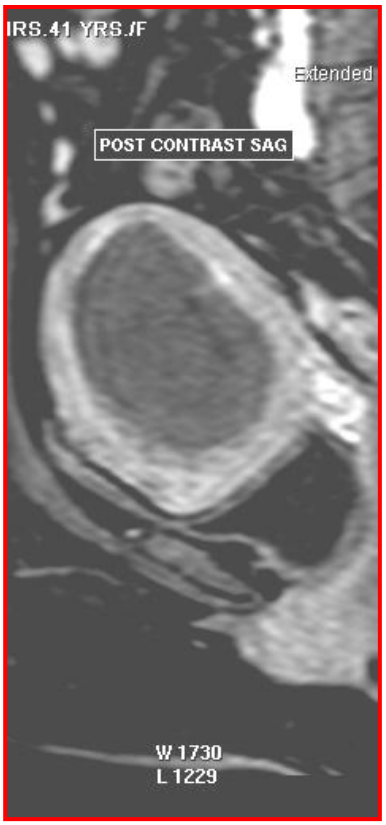
**Case 1:** Image (Left) - T2W preprocedure image showing a predominantly T2 hypointense anterior wall fibroid. Image (Right) – T1W post contrast image showing the non perfused area.




**Case 2**: Image (Left) - T2W preprocedure image showing a predominantly T2 hypointense anterior wall fibroid. Image (Right) – T1W post contrast image showing nearly 75%non-perfused volume.



**Case 3** : 52 year female who presented with menorrhagia pre and post procedure post contrast images showing the treated volume.


**Case 4**:41 year female who presented with frequent micturition, pre and post procedure post contrast images showing the T2 heterointense fibroid.

# RESULTS AND ANALYSIS

# RESULTS

## Demographic Data:

A total of 30 patients who underwent MR Guidedfocused ultrasound therapy for fibroids at Bharat Scans between January 2012 and December 2012 over a period of 12 months, who fit the inclusion criteria were enrolled in this study. They underwent a preliminary screening MRI and those who were found to be eligible on screening were included in the study.

The parameters measured were:

- Hematocrit.
- Menorrhagia scoring.
- Dysmenorrhea scoring.
- Pressure symptoms scoring.
- Immediate Nonperfused volume
- Fibroid volume and fibroid shrinkage.

These parameters were measured at 6months and at the end of 12 months. The efficacy of MRgFUS was defined as improvement in the haematocrit, symptom scoring and attaining >50%Nonperfused volume. Continuous data were represented by mean and standard deviation and categorical data were represented by frequencies and percentages and were analysed. A value of $p$ <0.05 was considered to be statistically significant. Data's were analysed with SPSS 14.0 version.

## TABLE – 1

## AGE DISTRIBUTION OF FIBROIDS

| Age Group | No. of Cases | Percent |
|---|---|---|
| 21 – 30 | 2 | 6.7 |
| 31 – 40 | 10 | 33.3 |
| 41 – 50 | 16 | 53.3 |
| 50 and above | 2 | 6.7 |

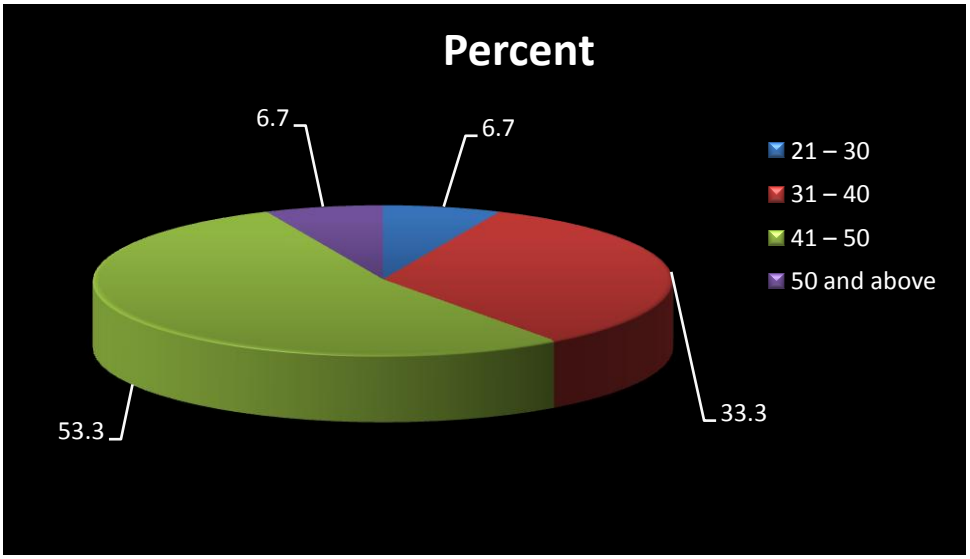



**Table 1** demonstrates age wise distribution of the sample size. Highest prevalence was observed between age 41 - 50 with 53.3% of patients which is consistent with the incidence of fibroids.

## TABLE 2

## FIBROID VOLUME DISTRIBUTION

| Fibroid volume range($cm^3$) | No. of Fibroids |
|---|---|
| < 100 | 5 |
| 100 – 200 | 10 |
| 200 – 300 | 11 |
| > 300 | 4 |

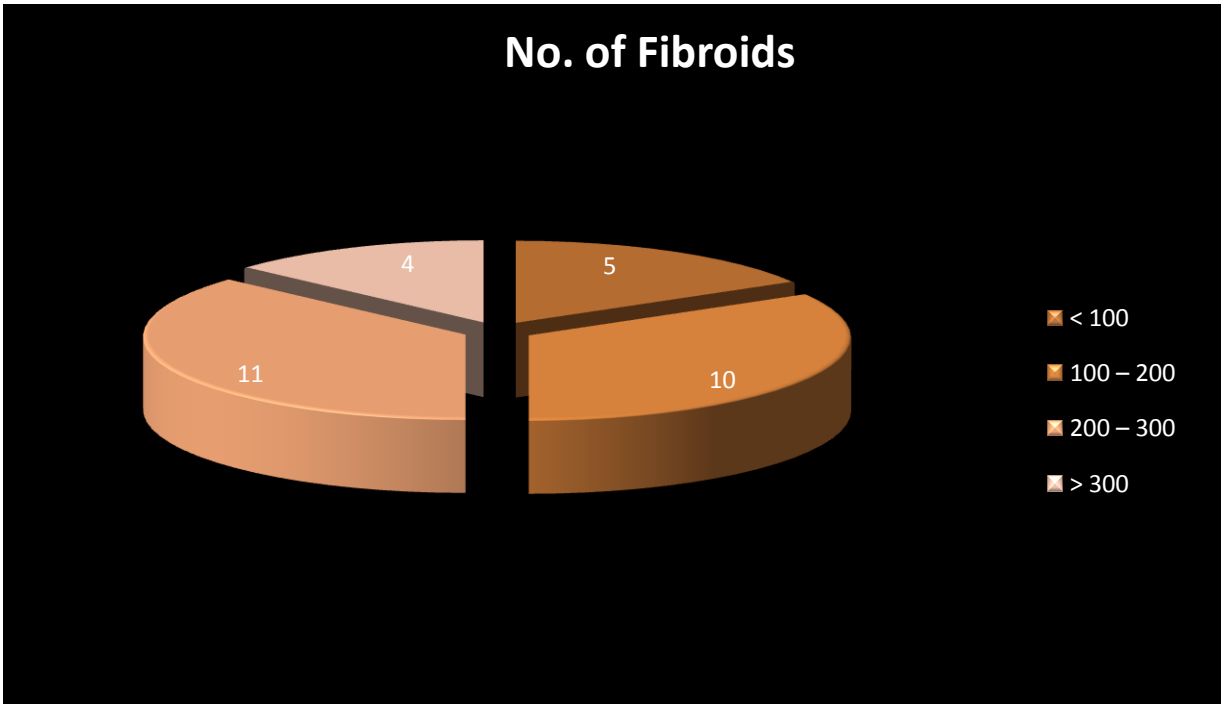



**Table 2** shows the distribution of fibroids as per their fibroid volume range. It was found that around 21 fibroids were in the range between 100 and 300 $cm^{3.}$

## TABLE – 3

## HEMATOCRIT PARIED SAMPLE STATISTICS

| | | Mean | N | Std. Deviation | Std. Error |
|---|---|---|---|---|---|
| Pair - I | HCT – Bef | 28.40 | 30 | 2.207 | 0.403 |
| | HCT – 6 mnths | 31.30 | 30 | 2.231 | 0.407 |
| Pair – II | HCT – Bef | 28.40 | 30 | 2.207 | 0.403 |
| | HCT – 12 mnths | 33.07 | 30 | 1.964 | 0.359 |

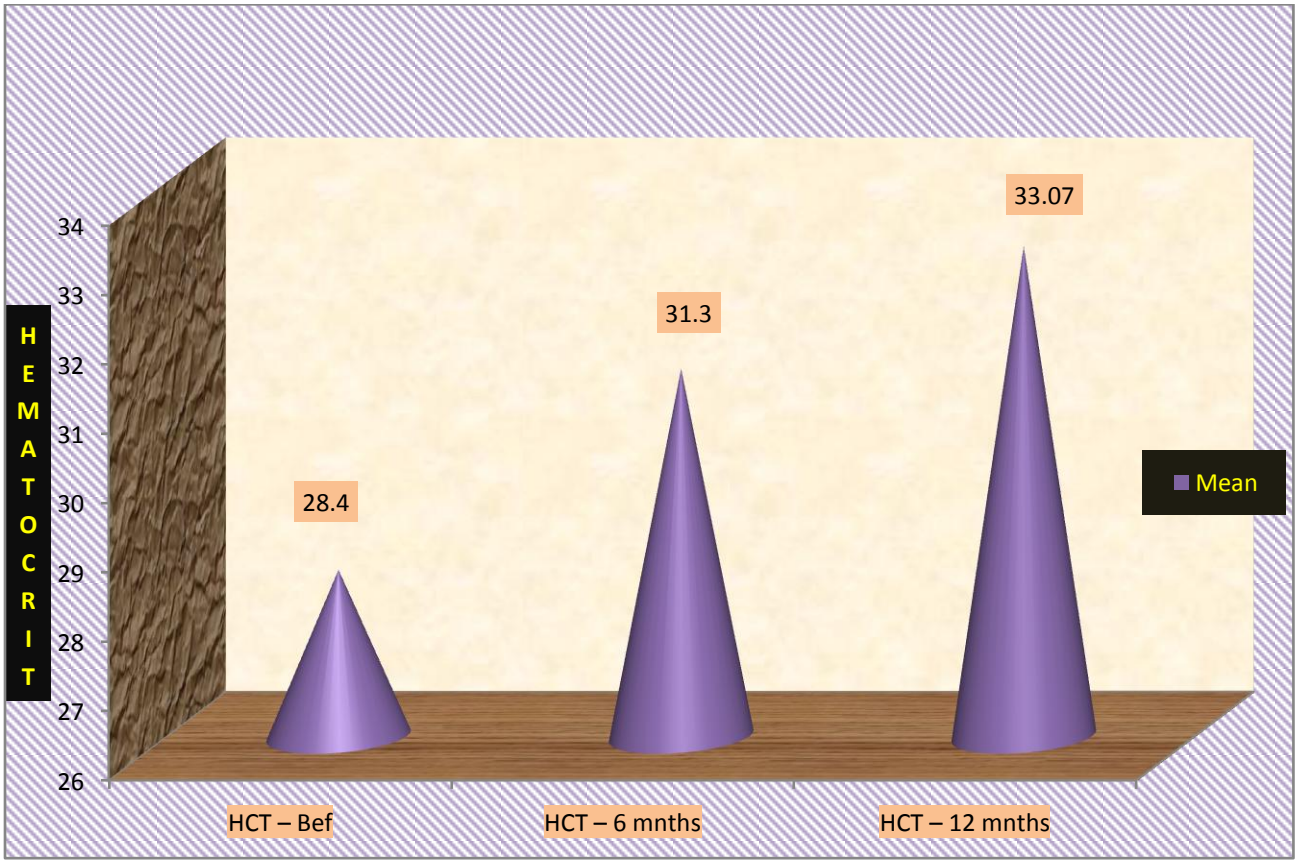



**Table 3** shows the mean baseline hematocrit and the gradual increase in the mean hematocrit at 6months and at 12 months after treatment. It has increased from 28.4 to 33.07.

## PAIRED SAMPLE TEST FOR HEMATOCRIT

| | | Mean | Std. Deviation | Std. Error Mean | p value |
|---|---|---|---|---|---|
| Pair - I | HCT – Bef | -2.900 | 1.296 | 0.237 | < 0.001 |
| | HCT – 6 mnths | | | | |
| Pair – II | HCT – Bef | -4.667 | 1.845 | 0.337 | < 0.001 |
| | HCT – 12 mnths | | | | |

The paired sample test between the hematocrit values before and after treatment at 6 months and 12 months showed a statistically significant increase with a p value of <0.001.

## TABLE 4,

## MENORRHAGIA SCORING – PAIRED SAMPLE STATISTICS

| | | Mean | N | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Pair - I | Men Score – Bef | 1.60 | 30 | 0.968 | 0.177 |
| | Men score – 6 months. | 0.40 | 30 | 0.563 | 0.103 |
| Pair – II | Men score – Bef | 1.60 | 30 | 0.968 | 0.177 |
| | Men score – 12 months | 0.17 | 30 | 0.379 | 0.069 |

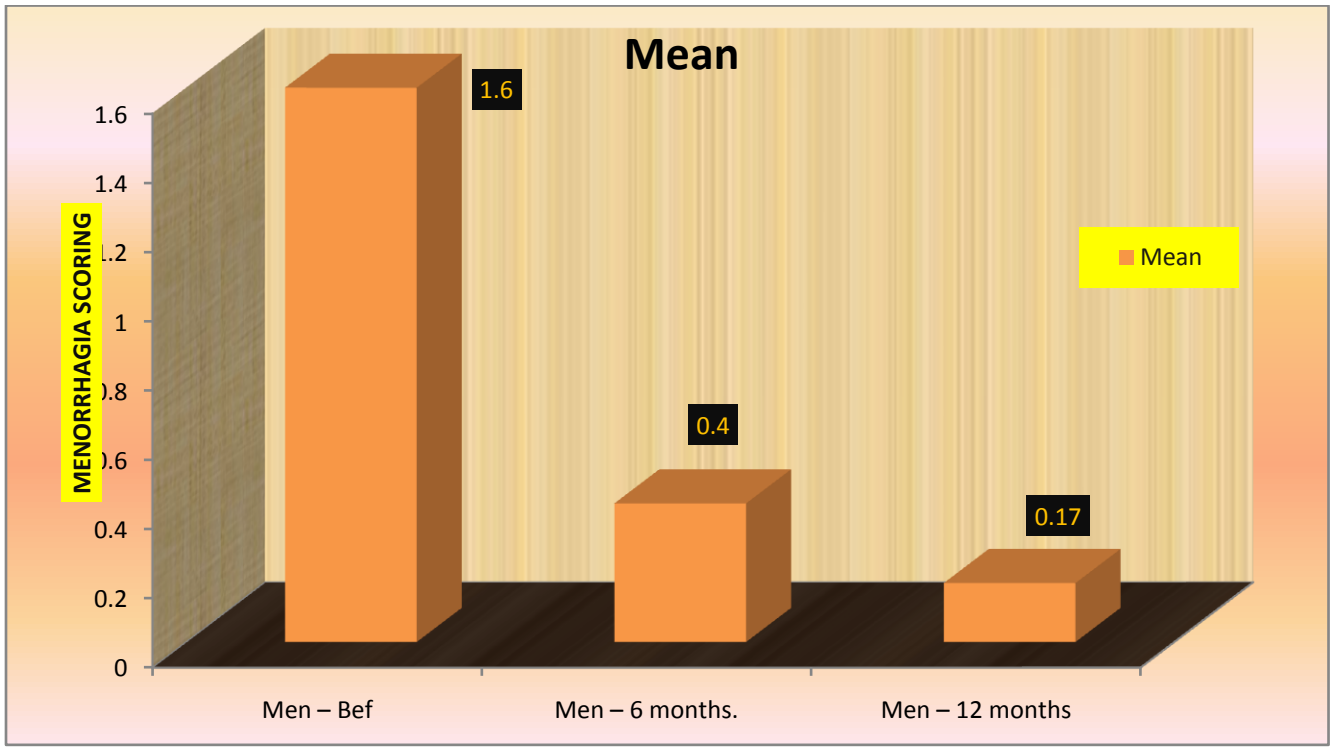



**Table 4** shows the mean menorrhagia score before and after treatment at 6 months and 12 months. There was a significant decline in the scoring with symptomimprovement.

**PAIRED SAMPLES TEST**

| | | **Mean** | **N** | **Std. Deviation** | **Std. Error Mean** | ***P value*** |
|---|---|---|---|---|---|---|
| Pair - I | Men score – Bef | 1.2 | 30 | 0.664 | 0.121 | *<0.001* |
| | Men score – 6 months. | | | | | |
| Pair – II | Men score – Bef | 1.433 | 30 | 0.817 | 0.149 | *<0.001* |
| | Men score – 12 months | | | | | |

The paired sample test between the mean menorrhagia scoring before and after treatment at 6 months and 12 months was done and was found to be statistically significant with a p value <0.001.

## TABLE 5

## DYSMENORRHEA SCORING

| | | Mean | N | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Pair - I | Dys Scoring – Bef | 2.13 | 30 | 0.629 | 0.115 |
| | Dys scoring– 6 months. | 0.80 | 30 | 0.714 | 0.130 |
| Pair – II | Dys scoring– Bef | 2.13 | 30 | 0.629 | 0.115 |
| | Dys scoring – 12 months | 0.27 | 30 | 0.450 | 0.82 |

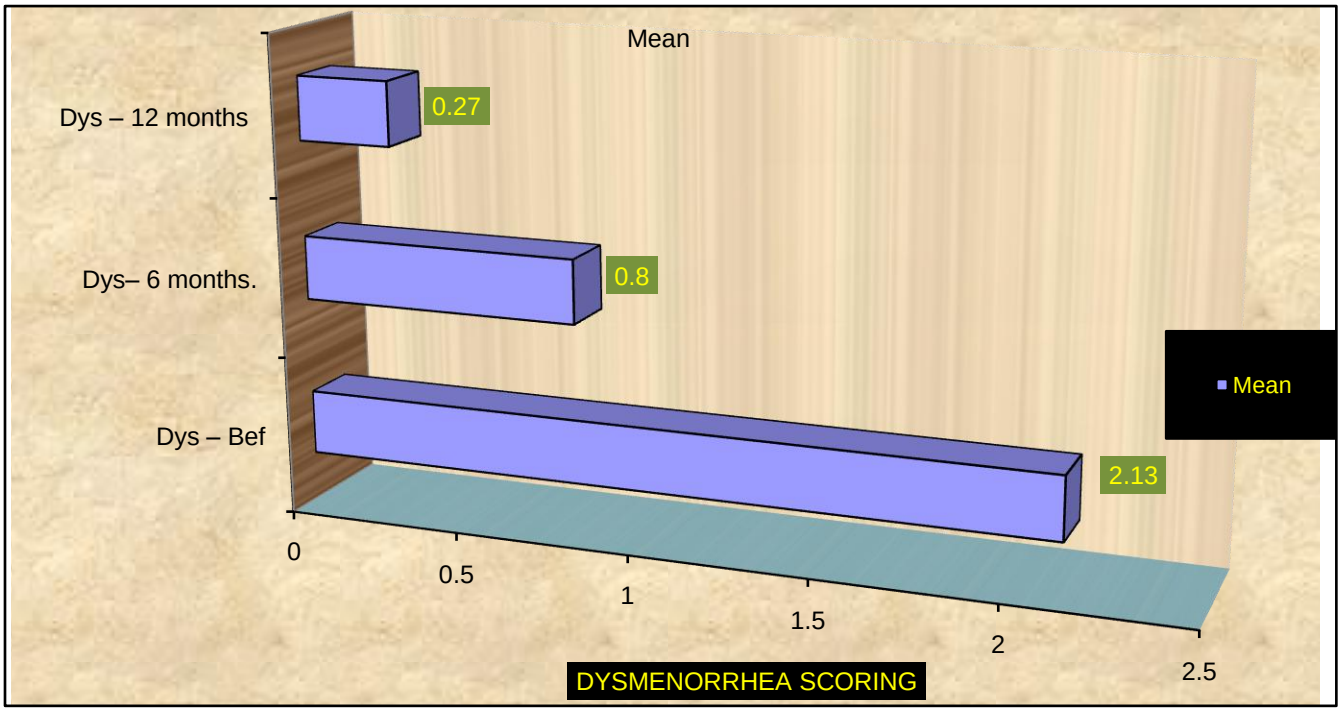



**Table 5**shows the mean dysmenorrhea score before and after treatment at 6 months and 12 months. There was a significant decline in the scoring with symptom improvement.

## PAIRED SAMPLE TEST FOR DYSMENORRHEA SCORING

| | | Mean | Std. Deviation | Std. Error Mean | P value |
|---|---|---|---|---|---|
| Pair - I | Dys – Bef | 1.333 | 0.479 | 0.088 | <0.001 |
| | Dys – 6 months. | | | | |
| Pair – II | Dys – Bef | 1.867 | 0.434 | 0.079 | <0.001 |
| | Dys – 12 months | | | | |

The mean baseline dysmenorrhea scoring decreased from 2.13 to 0.27.The paired sample The paired sample test between the mean dysmenorrhea scoring before and after treatment at 6 months and 12 months was done and was found to be statistically significant with a p value <0.001.

## TABLE 6

## PRESSURE SYMPTOMS PAIRED SAMPLE STATISTICS

| | | Mean | N | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Pair - I | Press symptoms scoring – Bef | 1.10 | 30 | 0.960 | 0.175 |
| | Press symptom scoring – 6 months. | 0.53 | 30 | 0.776 | 0.142 |
| Pair – II | Press symptom scoring – Bef | 1.10 | 30 | 0.960 | 0.175 |
| | Press symptom scoring – 12 months | 0.50 | 30 | 0.731 | 0.133 |

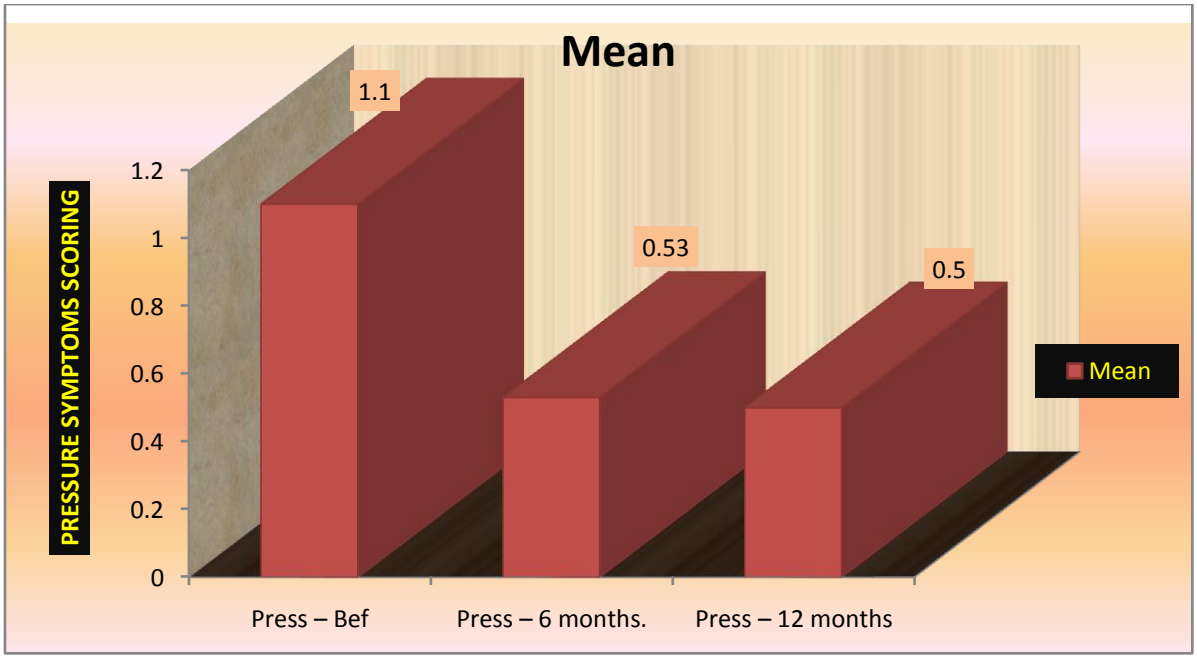



**Table 5** shows the mean dysmenorrhea score before and after treatment at 6 months and 12 months. There was a significant decline in the scoring with symptom improvement.

## PAIRED SAMPLE TEST

| | | Mean | Std. Deviation | Std. Error Mean | P value |
|---|---|---|---|---|---|
| Pair - I | Press sympt.- Bef | 0.567 | 0.568 | 0.104 | <0.001 |
| | Press sympt.- 6 months | | | | |
| Pair – II | Press sympt.- Bef | 0.600 | 0.563 | 0.103 | <0.001 |
| | Press sympt.- 12 months | | | | |

The mean baseline pressure symptom scoring decreased from1.10 to 0.5. The paired sample test between the mean pressure symptom scoring before and after treatment at 6 months and 12 months was done and was found to be statistically significant with a p value <0.001.

## TABLE 7

## MASS EFFECT CROSS TABULATION

| | | Mass Effect After | | Total |
|---|---|---|---|---|
| | | **No** | **Yes** | |
| **Mass effect Before** | **No** | 12 | 0 | **12** |
| | **Yes** | 8 | 10 | **18** |
| | **Total** | **20** | **10** | **30** |

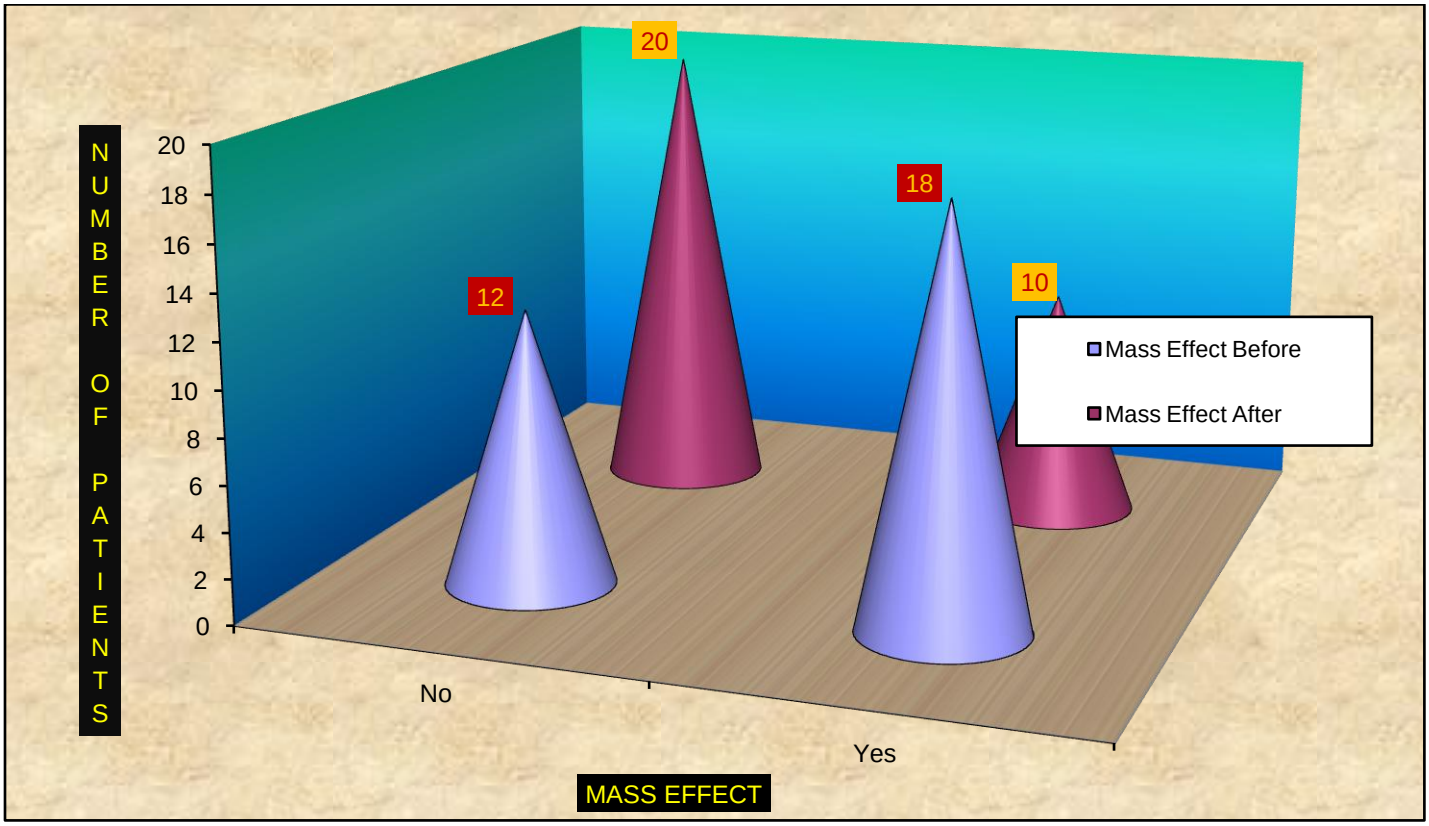



**Table 7** shows that out of 18 people who had mass effect before treatment, 8 were relieved of the symptom. But 10 of them had persistent symptoms.

# TABLE 8

## DISTRIBUTION OF IMMEDIATE NONPERFUSED VOLUME

| NPV Ratio (Immed.) | Mean | No. of fibroids | percentage |
|---|---|---|---|
| < 40% | 30.66 | 9 | 30 |
| 40 – 60% | 50.53 | 13 | 43.3 |
| > 60% | 65.75 | 8 | 26.7 |

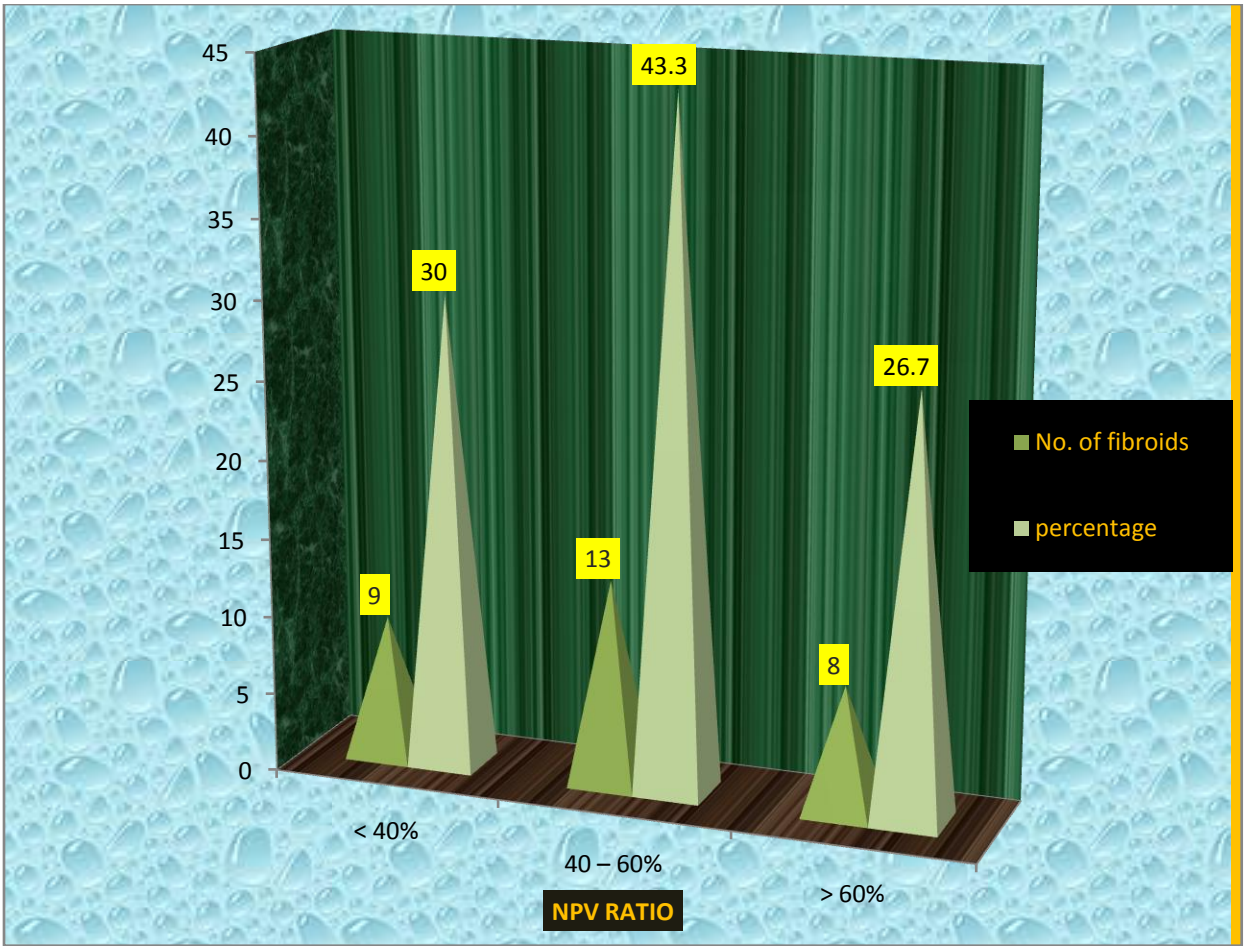



**Table 8** shows the distribution of NPV Ratio. Out of 30 patients treated, 43.3% of them attained between 40 and 60 % NPV Ratio, with a mean value of 48.98%

## TABLE 9

## FIBROID SHRINKAGE AND NPV

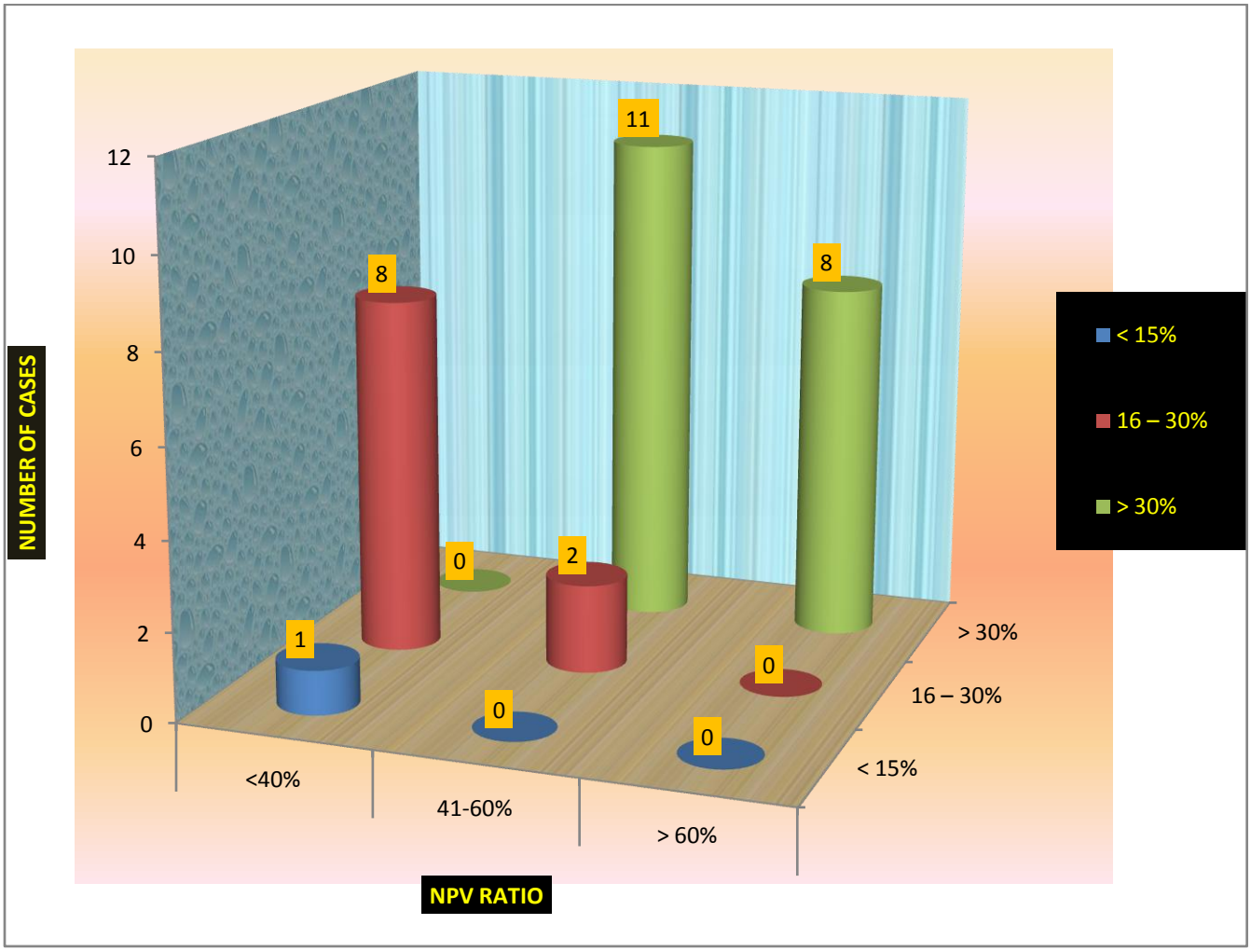
| FIBROID SHRINKAGE | NPV | | | | | |
|---|---|---|---|---|---|---|
| | <40% | | 41-60% | | > 60% | |
| < 15% | 1 | 100% | 0 | | 0 | |
| 16 – 30% | 8 | 80% | 2 | 20% | 0 | |
| > 30% | 0 | | 11 | 57.9% | 8 | 42% |
| | 9 | | 13 | | 8 | |

## CHISQUARE TEST

| | Value | df | Value |
|---|---|---|---|
| **Pearson chi-square** | 22.918 | 4 | |
| **Likelihood ratio** | 28.690 | 4 | < 0.001 |
| **Linear by linear Association** | 17.122 | 1 | |

**Table 9** shows that all fibroids that had a NPV ratio of >60% had a fibroid shrinkage of more than 30%.The values were analyzed with chi square tests and were found to have a significant p value of <0.001.

## RELATION BETWEEN NPV RATIO AND FIBROID SHRINKAGE




The above bar chart depicts that all 8 fibroids that had a NPV ratio of >60% and 11 out of 13 fibroids that attained a NPV ratio of 40-60% showed a fibroid Shrinkage of >30%.

# TABLE 10

## AGE GROUP AND NPV IMMEDIATE

| Age Group | No. of cases | < 40% | 40 – 60% | > 60% |
|---|---|---|---|---|
| < 35 Yrs. | 7 | 2 | 3 | 2 |
| 36 – 45 Yrs. | 16 | 3 | 8 | 5 |
| > 45 Yrs. | 7 | 4 | 2 | 1 |
| **Total** | **30** | **9** | **13** | **8** |

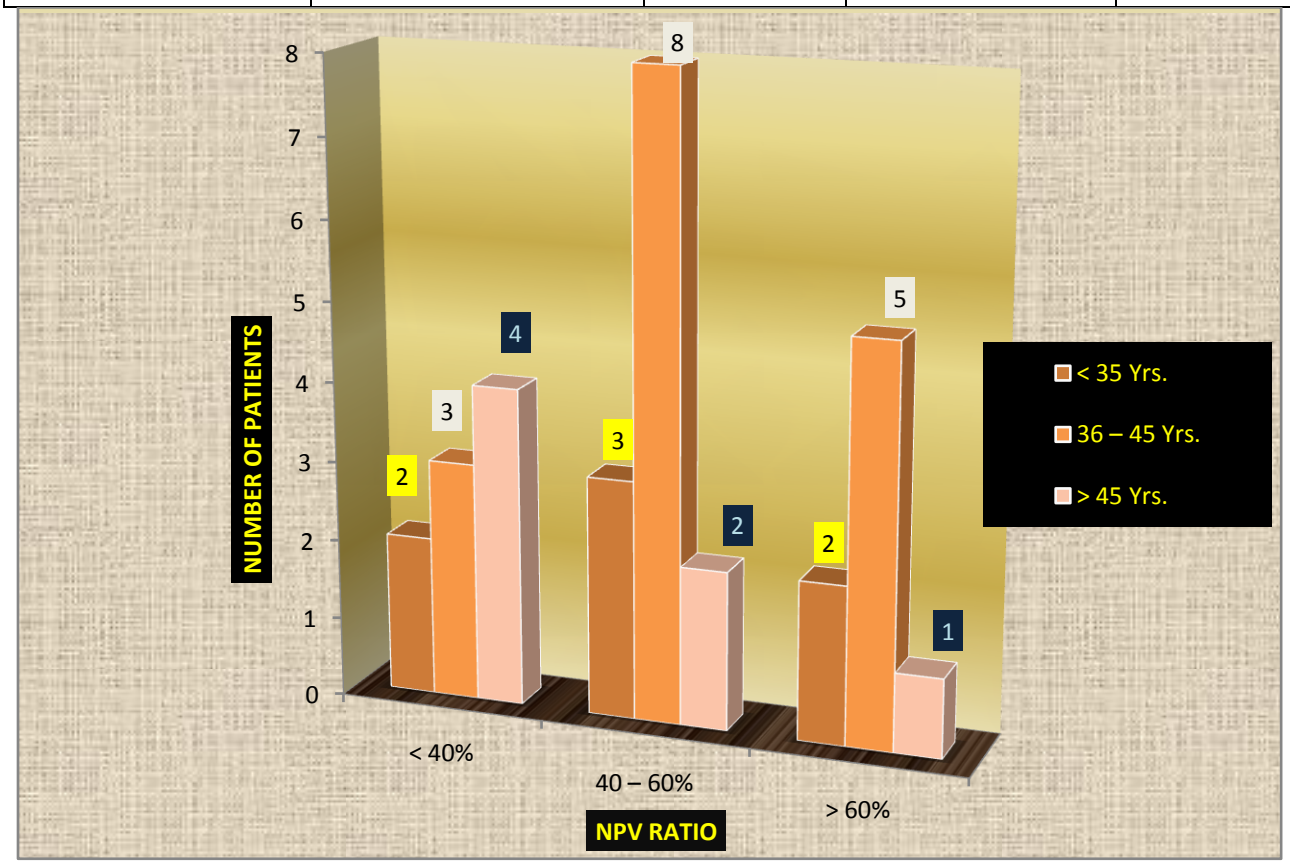



**Table 10** shows the distribution of NPV Ratio among different age groups. It is inferred that maximum NPV ratio is attained in the age group 36-45 years

# TABLE 11.

## ACOUSTIC WINDOW AND NPV

| Age Group | Total | < 40% | | 40 – 60% | | > 60% | |
|---|---|---|---|---|---|---|---|
| No Interference | 18 | 4 | (44.4) | 7 | (53.8) | 7 | (87.5) |
| Scar | 6 | 4 | (44.4) | 2 | (15.4) | 0 | (0) |
| Interference | 6 | 1 | (11.1) | 4 | (30.8) | 1 | (12.5) |
| **Total** | **30** | **9** | | **13** | | **8** | |

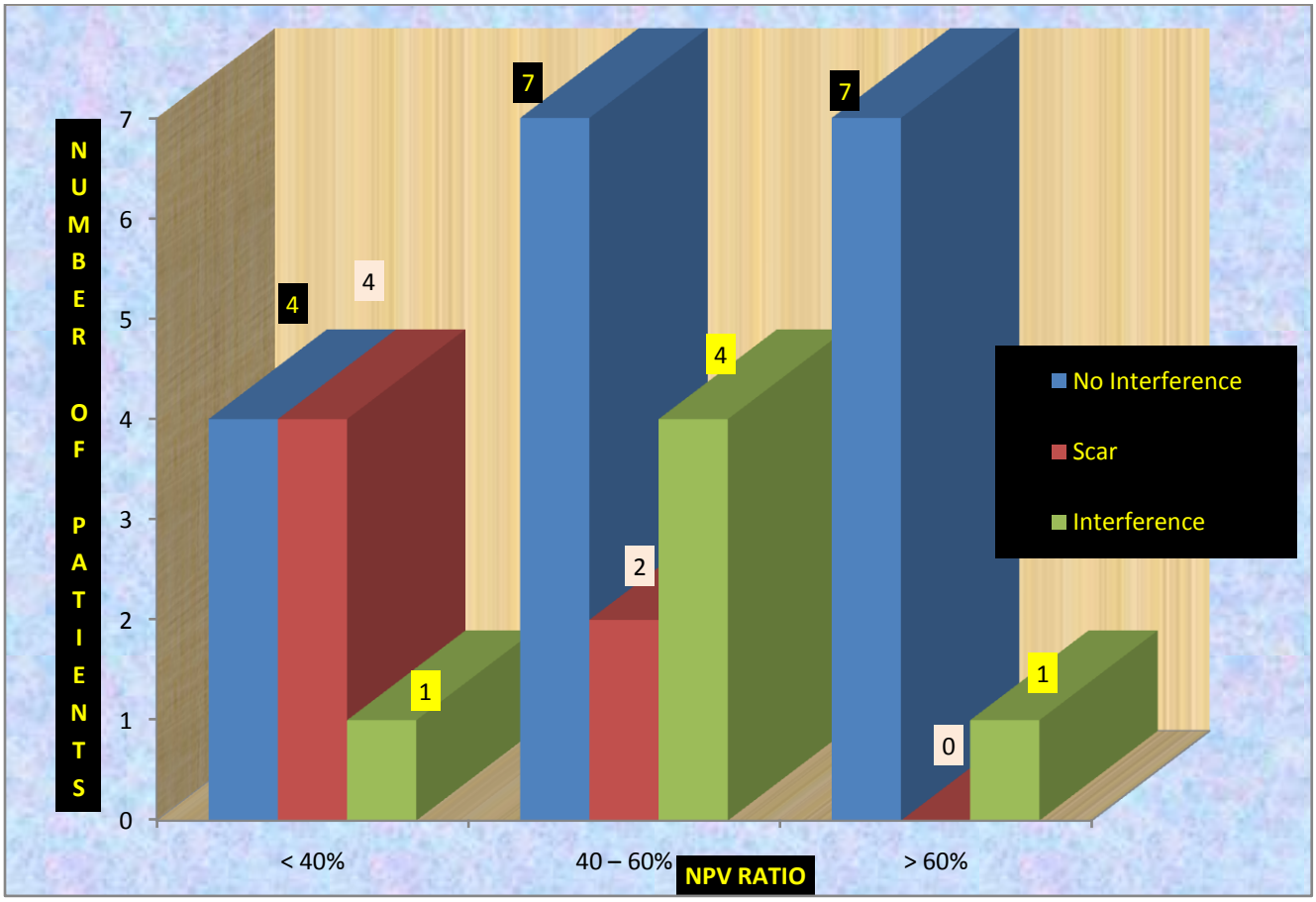



**Table 11** shows that 87.5% of patients who belonged to >60% NPV ratio had no interference in the beam pathway.

# TABLE 12

## NUMBER OF FIBROIDS AND NPV

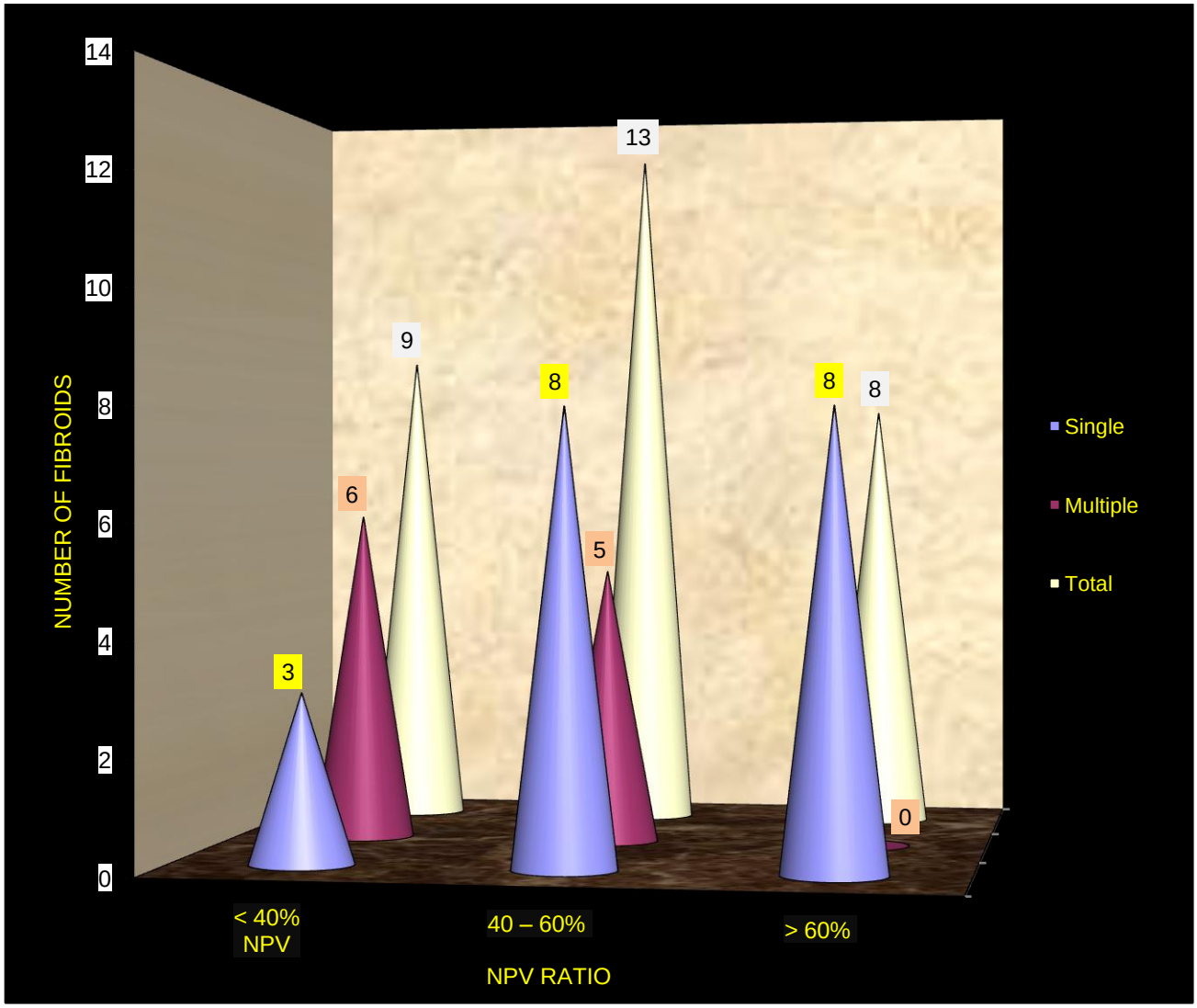
| No. of Fibroids | Total | NPV | | |
|---|---|---|---|---|
| | | < 40% | 40 – 60% | > 60% |
| Single | 19 | 3 | 8 | 8 |
| Multiple | 11 | 6 | 5 | 0 |
| **Total** | **30** | **9** | **13** | **8** |

**CHI-SQUARE TEST**

| | Value | Df | P value |
|---|---|---|---|
| **Pearson Chi-square** | 8.139 | 2 | 0.017 |

**Table12** shows the influence of the number of fibroids and NPV ratio. It shows that only single fibroids could attain a better NPV ratio. The analysis of the values gave a significant p value of <0.05.

## NUMBER OF FIBROIDS AND NPV




The bar chart depicts the relation between number of fibroids and NPV ratio. It was found that 100% of all fibroids that attained a NPV ratio of more than 60% were single fibroids.

## TABLE 13

## SIGNAL INTENSITY AND NPV

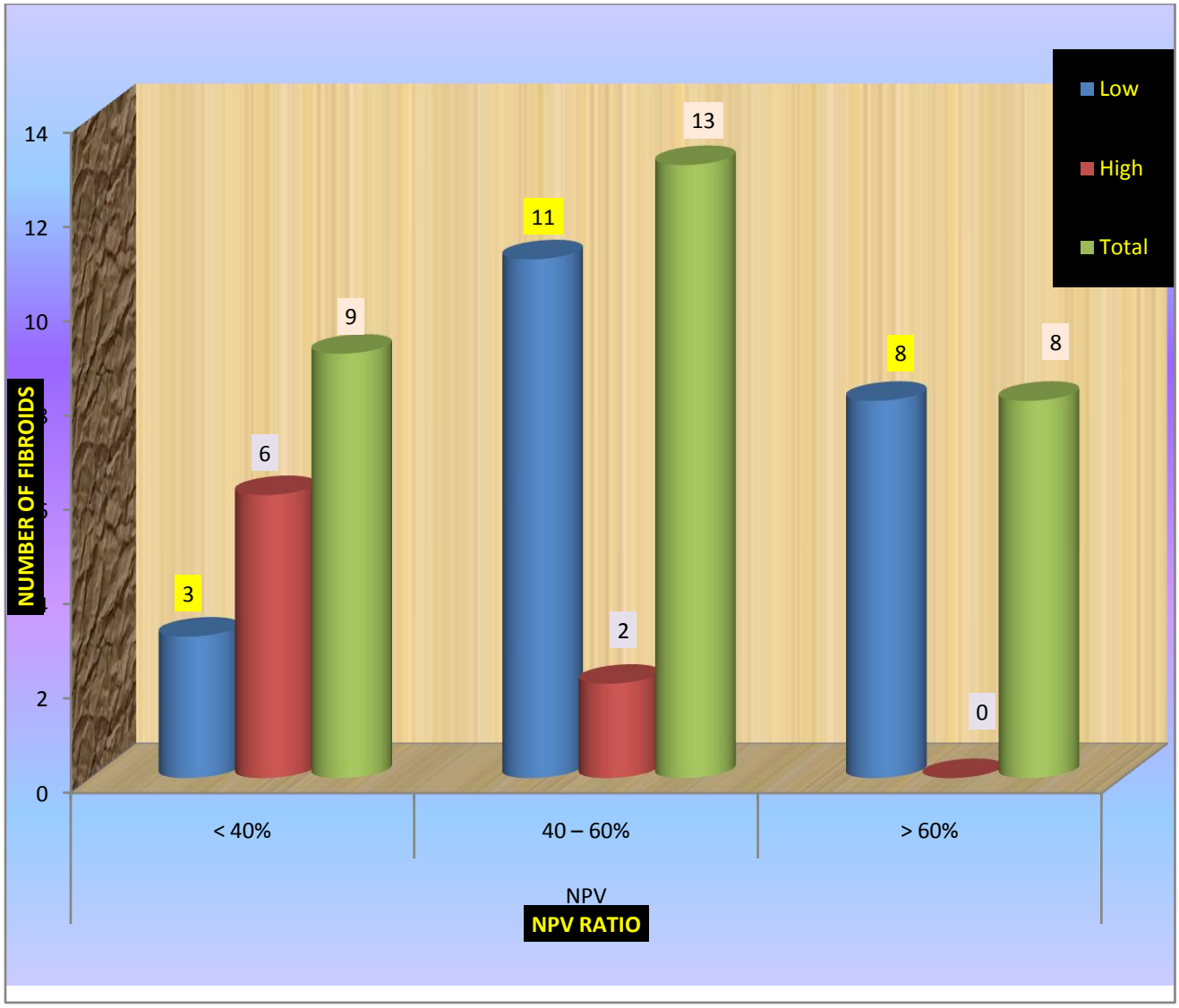
| Signal Intensity of fibroid | Total | NPV | | |
|---|---|---|---|---|
| | | **< 40%** | **40 – 60%** | **> 60%** |
| Low | 22 | 3 | 11 | 8 |
| High | 8 | 6 | 2 | 0 |
| **Total** | **30** | **9** | **13** | **8** |

## CHI-SQUARE TEST

| | **Value** | **Df** | **P value** |
|---|---|---|---|
| **Pearson Chi-square** | 11.119 | 2 | 0.004 |

**Table 13** shows the influence of signal intensity of fibroids on T2 weighted MR Images. It is inferred from the table that low intensity fibroids attain a better NPV ratio. The values were analyzed and was found to be significant with a p value of $<0.05$.

**Signal intensity of fibroid and NPV RATIO.**




The bar chart depicts the influence of signal intensity of fibroid with the NPV Outcome. It shows that 100% of >60% NPV was attained in low intensity fibroids, whereas 75% of high intensity fibroids attained NPV ratio of <40%.

## TABLE 14

## MRgFUS AND ADVERSE EFFECTS

| FIBROID VOLUME | NO. OF CASES | COMPLICATIONS | | NO COMPLICATIONS |
|---|---|---|---|---|
| | | FEVER | BACK PAIN | |
| <100 | 5 | 0 | 0 | 5 |
| 100-200 | 10 | 0 | 0 | 10 |
| >200 | 15 | 2 | 3 | 10 |
| | 30 | 2 | 3 | 25 |

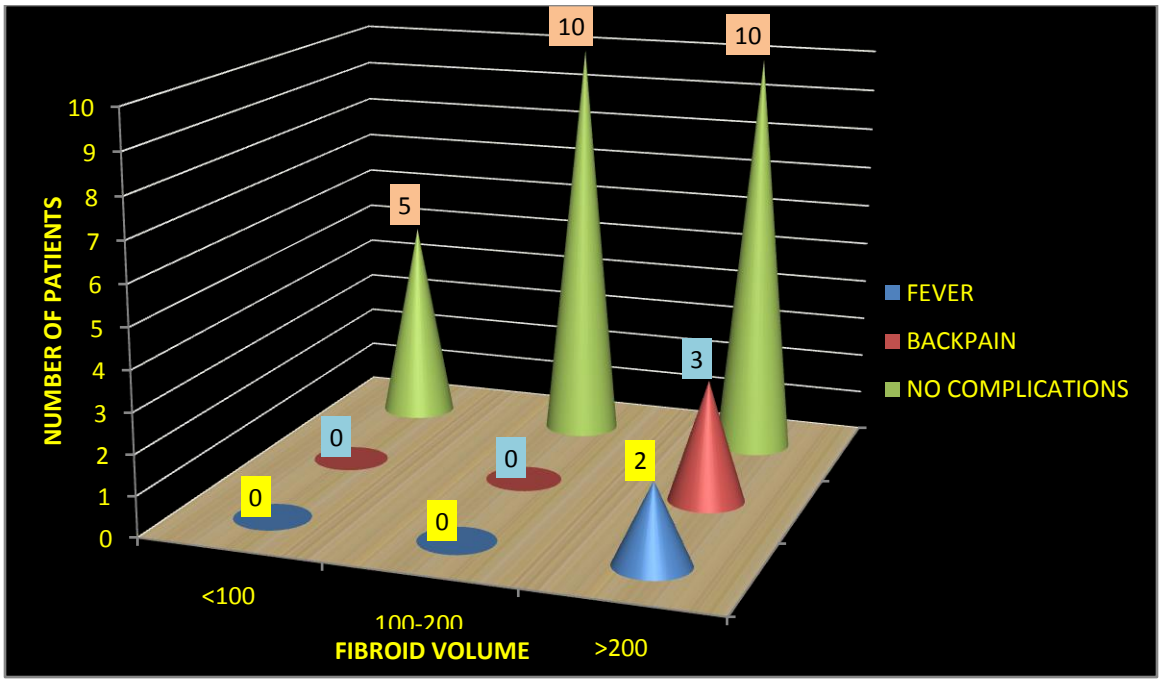



**Table 14** shows that out of 30 patients treated, five of them had minor adverse effects like fever and backpain.Adverse effects occurred in fibroids of volume >200$cm^3$ .

# TABLE 15

## MRgFUS AND ANY ADDITIONAL TREATMENT

| ANY ADDITIONAL TREATMENT | NO. OF FIBROIDS | PERCENT |
|---|---|---|
| YES | 2 | 6.7 |
| NO | 28 | 93.3 |

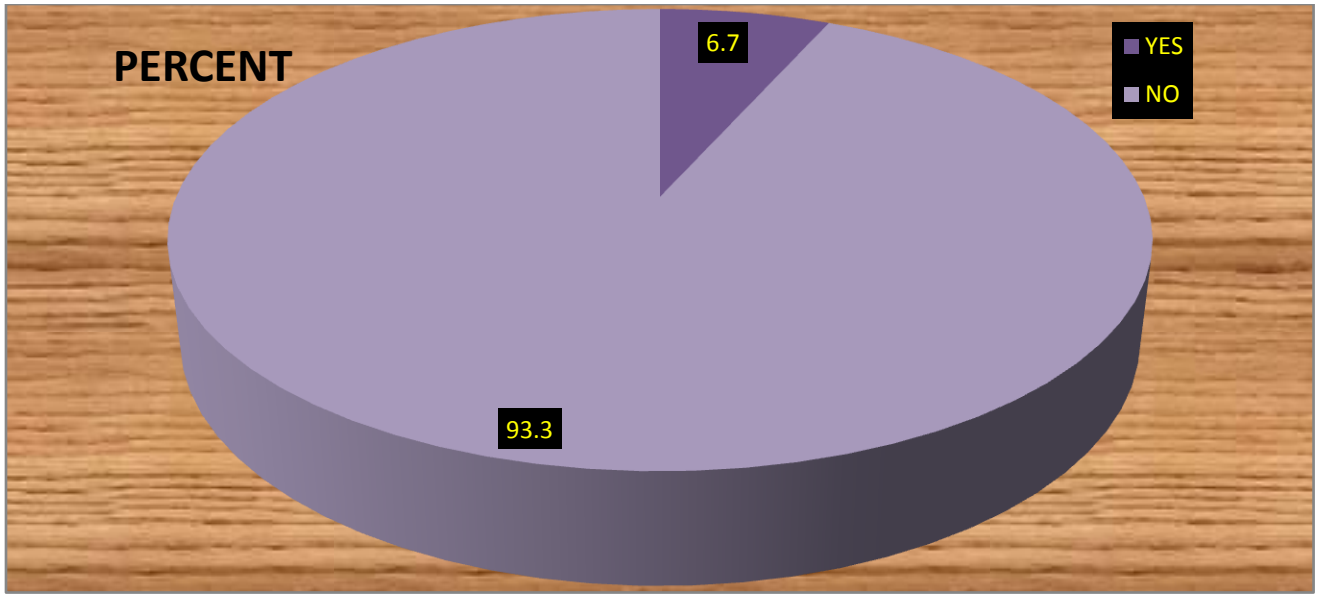



**Table 15** shows that out of 30 fibroids treated, two of them needed additional treatment of hysterectomy due to persistence of symptoms which comprised of 6.7% of fibroids treated.

# DISCUSSION

## DISCUSSION:

This is a prospective study conducted at the Institute of Social Obstetrics-Govt Kasturba Gandhi Hospital in collaboration with BHARATH SCANS during the period 2011-2012.

The purpose of this study was to assess the effectiveness of MRgFUS in the treatment of uterinefibroids. In our study we had 30 eligible patients with symptomatic fibroids who met the inclusion criteria and were enrolled after a preliminary MRI screening.

**Symptom severity scoring:**

Symptoms like menorrhagia,dysmenorrhea,pressuresymptoms and mass effect as reported by patients before,6 months and 12 months after treatment were assessed on a 4point scale with 0=none.1=mild,2=moderate and 3=severe.

The mean baseline for SSS OF MENORRHAGIA was

- At baseline:1.6
- At 6 months follow up:0.4
- At 12 months follow up:0.17

The mean values for SSS of DYSMENORRHEA was

- At baseline: 2.13
- At 6 months follow up:0.80
- At 12 months follow up: 0.27

The mean values for SSS of pressure symptoms were as follows:

Pressure symptoms

1. At baseline:1.10
2. At 6 months follow up: 0.53
3. At 12 months follow up: 0.50

All the above mentioned SSS showed a decline and had a statistical significance with pvalue <.001, hence proving the hypothesis that MRgFUS treatment brings about significant and sustained improvement in symptoms.

Stewart EA et al conducted a study in 2007 and concluded that the symptom severity scoring significantly reduced from the baseline as early as 3 months.[2]

Fenessey FM et al in 2007 showed that there was a significant 10 point improvement from baseline SSS score at the end of 12 months in those with NPV>30%[22].

Funaki K Sawadak et al in 2007 derived in his study of 63 patients that mean symptom scores were significantly reduced[35].

Rabinovici J Inbar Y Revel A et al in 2007 concluded that 69% of patients reported either significant or partial improvement in symptoms[36].

Gorny KR et al in 2011 conducted a study and showed that 92.9% of participants had symptom improvement at 6 months and 7.1% of them had no symptom relief[34].

**HEMATOCRIT:**

In our study there was a mean increase in hematocrit from the baseline which was attributed to significant reduction in menorrhagia.

The mean values for hematocrit in our study:

- Before:28.4
- At 6 months:31.3
- At 12 months:33.07

There was a statistically significant increase in hematocrit from a mean of 28.4 to 33.7 with a p value of <0.001.

Stewart EA et al,Rabinovici in 2007 showed higher symptom improvement and improvement in hematocrit with higher NPV ratio[33].

## FACTORS INFLUENCING IMMEDIATE NPV

### SIGNAL INTENSITY OF FIBROID:

In our study of 30 patients, we had 22 fibroids of low intensity and 8 fibroids of high intensity,

100 percent of >60% NPV and 84.6 percent of 41-60% NPV were of low intensity fibroids.

75percent of high intensity fibroids attained only <40% NPV.These values were coinciding well with a p value of <0.001.

Ronit et al in 2011 showed that hypointense fibroids had a better odd's ratio for a better NPV Ratio.

FunakiK, Fukunishi H.Funaki T et al in 2007 reported that the efficacy of MRgFUS correlates with the intensity of $T_2$ weightedimages. Hypointense fibroids are suitable whereas hyperintense are not[44].

Lanard ZM, Fenessey FM et al in 2008 showed that fibroids with low intensity were more likely to shrink[55].

Mikami et al in 2008 reported that treatment was unsuccessful in 33% of patients due to high signal intensity of fibroids[56].

**NUMBER OF FIBROIDS:**

In ourstudy, out of 30 patients, 19 were single fibroids and 11 were multiple fibroids.

100% of more than 60%NPV ratio was seen in single fibroids and 66.7% of <40% NPV ratio was seen in multiple fibroids.

Analysis of values showed a significant p value of <0.05.

**ACOUSTIC WINDOW**

Among 30 patients in our study,

18 patients had no interference in the acoustic window.

6 patients had scars and 6 patients had some interference in the beam pathway lie bowel, other viscera...

87.5% of >60% NPV ratio was attained only when there was no interference in the beam pathway.83% of NPV ratio <40% had some kind of interference in theform of scars, bowel or other viscera.

Le Blang SD et al 2010 reported that factors limiting ablation were obstacles to passage of ultrasound beam like scars, bowel[39].

## NONPERFUSED VOLUME RATIO.

The mean NPV ratio attained from a sample of 30 patients in our study is 48± 14%.This is influenced by many factors like signal intensity of fibroid, number of fibroids, depth of fibroids and interference in the acoustic window.

The Immediate NPV ratio attained correlated well with the symptom improvement and fibroid shrinkage.

Okada A et al in 2009 reported a mean NPV ratio of 46.6%[36].

GornyKR et al in 2011 showed an immediate NPV Ratio of 45.4%[38].

LeBlang SD et al in 2010 reported in his study a mean NPV ratio of 55%[39].

## FIBROID SHRINKAGE

In our study the mean shrinkage of fibroid by the end of 6 months was 32%.These values correlated well with the IMMEDIATE NPV RATIO.

The values were analyzedwith chi square tests and were found to have a significant p value of <0.05.

Le Blang SD et al in 2010 reported in his study a mean fibroid shrinkage of 31%[39].

LinYH, Leung TK, Wang HJ et al in 2009 showed that fibroid reduction by 6 months was 30.8%[57].

RenXL Zhang J et al in 2007 reported a mean reduction in size of fibroid of about 49% by the end of 12 months[58].

**ADVERSE EVENTS**

Out of 30 patients who underwent MRgFUS in our study, five of them reported minor adverse effects like fever, back pain.

Two patients had fever which comprised of 6.6%.

Three patients had back pain which comprised of 10% of patients. There was no incidence of skin burns, sciatic nerve palsy.

Taran FA et al in 2009 reported in his study of incidence of 2.8% of fever[34].

Okada A et al in2009 reported post procedure adverse events as follows:[36]

Low back pain-8%, fever-6%, skin burns-1%, vaginal discharge-8%.

Le Blang SD et al in 2010 showed that the incidence of minor skin burns was 2.5% and sciatica was 1.2%[39].

## ANY ADDITIONAL TREATMENT

Among 30 patients in our study, twoof them opted out and went in for hysterectomy due to persistent symptoms especially because of the mass effect since the size of uterus was more than 16 weeks. This comprises of 6.6%.The hysterectomy specimen showed vast areas of necrosis.

Taran FA et al in2009 reported a treatment failure rate of 3.7%[34]

Okada A et al showed that the rate of alternative treatment by the end of 12 months was 5%[36].

Fenessey FM et al in 2007 showed that 28% sought alternative treatment[37].

Gorny KR et al in 2011 reported that additional procedures for fibroid related symptoms within 1 year was 6.2%[38].

# SUMMARY

## SUMMARY:

- The sample studied was 30 women with symptomatic fibroids.
- Of these 19 had single fibroids and 11 had multiple fibroids.
- 22 were of low intensity and 8 were of high intensity fibroids on $T_2$ weighted MR images.
- There was a statistically significant decline in the symptom severity as per the symptom severity scoring for menorrhagia,dysmenorrhea,pressure symptoms and mass effect and pelvicdiscomfort.
- There was a statistically significant improvement in the mean hematocrit.The mean hematocrit increased from 28.4 to 33.07 with a significant p value of <0.001.
- The mean NPV ratio attained in our study was 48.63$\pm$14% which was comparable with that o other previous studies.
- The mean fibroid shrinkage attained by 6 months was about 32% which correlated well with the immediate NPV Ratio with a significant p value <0.001.
- Factors influencing NPV ratio were found to be signal intensity of fibroids, number of fibroids and any interference in the pathway of the ultrasound beam.

# CONCLUSION

# CONCLUSION

MRgFUS has been tested and approved by the FDA and is a very successful noninvasive therapy particularly in those who demand a minimum treatment recovery time and for those who are unfit for anesthesia and surgery due to other comorbid medical illness.

- From our study, there is evidence of improvements in the symptoms in patients treated with the MRgFUS, particularly for those presenting with symptoms of menorrhagia and dysmenorrhea. The symptom relief was sustained till one year.
- Our study also showed a substantial improvement in the hematocrit following the procedure.
- The mean fibroid shrinkage at 6 months correlated well with the immediate Nonperfused volume obtained.
- In respect of safety, MRgFUS resulted in very minor adverse events like fever, abdominaldiscomfort, and backpain. There were no serious complications.
- Women typically were able to return to their normal daily activities the following day.
- In our study,there was no recurrence demonstrated and about 6.7% of them underwent hysterectomy due to persistent pressure symptoms.

**In conclusion, our data shows that MR-guided focused US is an effective technique to noninvasively and safely treat uterine leiomyomas in eligible patients, and it delivers significant and lasting symptom relief.**

**LIMITATIONS OF OUR STUDY:**

- Smaller sample size
- This sample population does not represent the true population.
- Follow up period is 12 months and hence durability of symptoms could not be proved beyond 12 months.
- Moreover there is no control group and whatever bias that may have existed in the patient selection is not known.

Nonetheless the results are encouraging and further evaluation with different protocols is definitely warranted.

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# ***ABBREVIATIONS***

**MRgFUS** – Magnetic Resonance guided Focused Ultrasound

**HIFU**-High Intensity Focused Ultrasound

**SSS** – Symptom Severity Score

**USG** – Ultrasonogram

**NPV** – Non Perfused Volume

**MRI**- Magnetic Resonance Imaging

**UAE**- Uterine Artery Embolisation

**FUS-**Focused UltraSound

## MASTER CHART

| SERIAL NO. | NAME | AGE | I.P.No. | BMI | SIZE OF UTERUS | ACOUSTIC WINDOW | NUMBER OF FIBROIDS | SIGNAL INTENSITY OF FIBROID | DURATION OF TREATMENT MIN | FIBROID VOLUME-BEF | FIBROID VOLUME-AFT | FIBROID SHRINKAGE | HEM-BEF | HEM-6mths | HEM-12mths | MEN-BEF | MEN-6mths | MEN-12mths | DYS-BEF | DYS-6mths | DYS-12mths | PRES SYMP-BEF | PRES SYMP-6mths | PRES SYMP-12mths | MAS EFF BEF | MAS EFF-AFT | NPV-IMMED | RETURN TO WORK IN DAYS | ANY ADD.L TREATMENT | ANY COMPLICATIONS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Sarojini | 40 | 839 | 30 | 8 | NIL | Single | LOW | 105 | 59 | 36 | 40 | 27 | 32 | 33 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | N | N | 65 | 1 | NIL | NIL |
| 2 | Punithavathi | 45 | 1691 | 32 | 10 | INT | Multiple | LOW | 135 | 68 | 61 | 25 | 33 | 36 | 36 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | N | N | 32 | 1 | NIL | NIL |
| 3 | Yamuna | 48 | 1213 | 32 | 10 | NIL | Single | HIGH | 185 | 79 | 68 | 28 | 28 | 33 | 35 | 3 | 1 | 0 | 2 | 1 | 0 | 2 | 2 | 2 | Y | Y | 34 | 1 | NIL | NIL |
| 4 | Suseela | 45 | 1631 | 29 | 10 | NIL | Single | LOW | 165 | 88 | 77 | 44 | 31 | 33 | 36 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | N | N | 75 | 1 | NIL | NIL |
| 5 | Sundari | 32 | 664 | 25 | 10 | NIL | Single | LOW | 80 | 98 | 84 | 29 | 30 | 32 | 32 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | N | N | 42 | 1 | NIL | NIL |
| 6 | Jayaseeli | 29 | 1104 | 23 | 10 | INT | Multiple | LOW | 105 | 108 | 89 | 27 | 30 | 30 | 30 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | N | N | 33 | 1 | NIL | NIL |
| 7 | Rajeswari | 45 | 763 | 31 | 12 | NIL | Single | LOW | 190 | 123 | 101 | 37 | 28 | 30 | 32 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | N | N | 58 | 1 | NIL | NIL |
| 8 | Poongothai | 34 | 1056 | 28 | 12 | NIL | Single | LOW | 90 | 132 | 98 | 37 | 26 | 30 | 33 | 2 | 0 | 0 | 2 | 1 | 0 | 1 | 0 | 0 | Y | N | 63 | 1 | NIL | NIL |
| 9 | Sumithra | 38 | 1605 | 28 | 12 | NIL | Single | LOW | 160 | 149 | 101 | 42 | 30 | 32 | 35 | 2 | 0 | 0 | 3 | 2 | 1 | 1 | 0 | 0 | Y | N | 71 | 1 | NIL | NIL |
| 10 | Nagalakshmi | 45 | 479 | 30 | 14 | INT | Multiple | LOW | 145 | 161 | 104 | 29 | 28 | 30 | 30 | 3 | 1 | 1 | 3 | 2 | 1 | 3 | 1 | 1 | Y | N | 41 | 1 | NIL | NIL |
| 11 | Umarani | 41 | 1607 | 31 | 14 | NIL | Single | LOW | 200 | 178 | 112 | 37 | 28 | 31 | 33 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | N | N | 56 | 1 | NIL | NIL |
| 12 | Kalaiarasi | 43 | 991 | 31 | 14 | NIL | Single | LOW | 170 | 182 | 119 | 34 | 30 | 33 | 33 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | Y | N | 42 | 1 | NIL | NIL |
| 13 | Stella | 48 | 1302 | 31 | 12 | INT | Single | LOW | 170 | 186 | 118 | 36 | 28 | 32 | 34 | 2 | 1 | 0 | 3 | 1 | 1 | 2 | 1 | 1 | Y | Y | 43 | 1 | NIL | NIL |
| 14 | Hemavathi | 34 | 1276 | 25 | 12 | NIL | Single | LOW | 125 | 194 | 126 | 37 | 30 | 33 | 36 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | N | N | 62 | 1 | NIL | NIL |
| 15 | Dhanam | 45 | 1209 | 30 | 12 | NIL | Single | HIGH | 180 | 199 | 123 | 22 | 30 | 30 | 33 | 1 | 1 | 0 | 2 | 1 | 1 | 0 | 0 | 0 | N | N | 27 | 1 | NIL | NIL |
| 16 | Shamsudha | 41 | 1502 | 32 | 12 | INT | Single | LOW | 210 | 212 | 138 | 28 | 29 | 33 | 36 | 2 | 0 | 0 | 2 | 1 | 0 | 1 | 0 | 0 | Y | N | 38 | 1 | NIL | NIL |
| 17 | Lalitha | 40 | 1158 | 29 | 14 | NIL | Single | LOW | 150 | 229 | 147 | 36 | 33 | 36 | 36 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | N | N | 54 | 1 | NIL | NIL |
| 18 | Nalina | 23 | 1403 | 29 | 18 | NIL | Multiple | HIGH | 180 | 233 | 193 | 32 | 27 | 28 | 30 | 2 | 1 | 1 | 3 | 2 | 1 | 2 | 2 | 1 | Y | Y | 46 | 2 | NIL | NIL |
| 19 | Famidha | 46 | 1305 | 33 | 14 | NIL | Multiple | HIGH | 130 | 235 | 152 | 24 | 27 | 32 | 32 | 3 | 1 | 1 | 3 | 2 | 1 | 1 | 1 | 1 | Y | Y | 31 | 1 | NIL | NIL |
| 20 | Mehboob | 47 | 1134 | 33 | 14 | ,INT | Multiple | HIGH | 200 | 249 | 168 | 27 | 30 | 33 | 35 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | N | N | 33 | 1 | NIL | NIL |
| 21 | Kamala | 35 | 332 | 22 | 16 | SC | Multiple | HIGH | 165 | 252 | 182 | 13 | 25 | 28 | 30 | 3 | 2 | 1 | 2 | 1 | 0 | 3 | 2 | 2 | Y | Y | 22 | 2 | NIL | Backpain |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 22 | Pushpa | 48 | 1182 | 33 | 14 | NIL | Multiple | HIGH | 195 | 261 | 174 | 19 | 30 | 33 | 33 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | N | N | 26 | 1 | NIL | NIL |
| 23 | Renuka | 52 | 1257 | 31 | 16 | NIL | Single | LOW | 180 | 265 | 212 | 37 | 28 | 33 | 33 | 1 | 0 | 0 | 2 | 1 | 0 | 1 | 0 | 0 | Y | N | 61 | 1 | NIL | NIL |
| 24 | Saradha | 43 | 1648 | 30 | 16 | NIL | Single | LOW | 180 | 274 | 192 | 38 | 30 | 32 | 33 | 1 | 0 | 0 | 2 | 1 | 0 | 1 | 0 | 0 | Y | N | 68 | 1 | NIL | NIL |
| 25 | Gandhimathi | 42 | 1510 | 30 | 16 | NIL | Single | LOW | 135 | 288 | 216 | 34 | 27 | 30 | 33 | 1 | 0 | 0 | 2 | 1 | 0 | 1 | 0 | 0 | Y | N | 46 | 1 | NIL | FEVER |
| 26 | Shantha | 40 | 467 | 29 | 18 | SC | Multiple | HIGH | 195 | 292 | 228 | 35 | 26 | 28 | 30 | 3 | 1 | 1 | 3 | 1 | 1 | 3 | 2 | 2 | Y | Y | 57 | 2 | NIL | Backpain |
| 27 | Gopika | 44 | 1196 | 31 | 18 | SC | Single | LOW | 175 | 302 | 254 | 34 | 26 | 30 | 33 | 2 | 0 | 0 | 2 | 0 | 0 | 2 | 1 | 1 | Y | Y | 61 | 1 | NIL | Backpain |
| 28 | Buela | 33 | 1007 | 26 | 20 | SC | Multiple | LOW | 220 | 304 | 221 | 33 | 24 | 27 | 31 | 3 | 1 | 0 | 3 | 2 | 1 | 2 | 1 | 1 | Y | Y | 56 | 2 | NIL | NIL |
| 29 | Kavipriya | 40 | 1721 | 25 | 18 | SC | Single | LOW | 175 | 314 | 269 | 36 | 28 | 31 | 34 | 2 | 1 | 0 | 3 | 1 | 0 | 1 | 1 | 1 | Y | Y | 59 | 2 | HYST. | NIL |
| 30 | Sasikala | 53 | 1227 | 30 | 20 | SC | Multiple | LOW | 200 | 326 | 265 | 33 | 25 | 28 | 32 | 3 | 1 | 0 | 2 | 1 | 0 | 2 | 2 | 2 | Y | Y | 57 | 2 | HYST. | FEVER |

***KEY TO MASTER CHART***

**Scoring system for pain:**

None – 0

Mild – 1

Moderate – 2

Severe – 3

DYS – Dysmenorrhoea

MEN- Menorrhagia

PRESS – Pressure symptoms

HCT – Hematocrit

TOT – Total Score

FIN - Final

Bef – BeforeAft– After

HEM-HEMATOCRIT

HYST-HYSTERECTOMY

INT-INTERFERENCE

# ANNEXURES

## ***PROFORMA***

Name

Age

IP Number

Socio economic status

Address

Obstetric score

LMP:

**Menstrual History**: before/after

MENORRHAGIA-None/Mild/Moderate/Severe

DYSMENORRHEA- None/Mild/Moderate/Severe

**Other symptoms**: before/after

PRESSURE SYMPTOMS –None/Mild/Moderate/Severe

MASS EFFECT - yes/no

Marital History

Obstetric History

Past History

## ***GENERAL EXAMINATION***

Temperature

Pulse

BP

BMI

Anemia

Pedal edema

Breast

Thyroid

Spine

**Per abdomen:**

Presence of scars

Type of scar

**Bimanual pelvic examination:**

Size of uterus

Single/multiple fibroids

**INVESTIGATIONS:**

- Basic routine investigations esp Hematocrit—before/after
- Urine pregnancy test
- Ultrasound pelvis
- Colposcopy
- MRI pelvis

  Fibroid volume

Number of fibroids

Any interference in the acoustic window

Signal intensity of fibroid

## பகுதி II

### சுய ஒப்புதல் படிவம்

### ஆய்வு செய்ப்படும் தலைப்பு

(MRI ஸ்கேன் உதவியுடன் அல்ட்ராசோனிக் அதிர்வுகள் மூலம் கர்பப்பையில் ஏற்படும் பைப்ராய்டு எனும் கட்டியை அகற்றுதல் தொடர்பான ஆய்வு)

ஆய்வு செய்யும் இடம் : சமூக மகப்பேறியல் மற்றும் அரசு கஸ்தூரிபாய் காந்தி தாய்சேய் நல மருத்துவமனை, சென்னை மருத்துவக் கல்லூரி, சென்னை

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் எண்:

பங்கு பெறுபவரின் வயது :

பங்கு பெறுபவர் இதனை ( ) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாக என்னுடைய உடல்நிலை குறித்த தகவல்களை ஆய்வு மேற்கொள்ளும் போது இந்த ஆய்வில் பங்குபெறும் மருத்துவர், ஆய்வு மேற்கொள்ளும் நிறுவனம், நன்நடத்தை நெறிமுறைகள் குழு, ஒழுங்குமுறை ஆணையங்கள் ஆகியவர்கள் காண என் முழுமனதுடன் சம்மதிக்கிறேன். நான் ஆய்விலிருந்து விலகி கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையோ, முடிவுகளையோ அறிவியல் சார்ந்த தேவைகளுக்காக பயன்படுத்திக்கொள்ள மறுக்கமாட்டேன். மூணாம் நபர்களுக்கு தரப்படும் அல்லது பிரசுரிக்கப்படுத் ஏதேனும் தகவல்களில் என் தனிப்பட்ட அடையாளம் வெளிப்படுத்தப்படமாட்டாது எனவும் நான் புரிந்து கொண்டேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் .....இடம் .....தேதி

கட்டைவிரல் ரேவை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் .....இடம் .....தேதி

ஆய்வாளரின் பெயர் .....

# INFORMED CONSENT FORM

PART II

STUDY TITLE

PROSPECTIVE STUDY ON THE EFFECTIVENESS OF MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND THERAPY IN THE TREATMENT OF UTERINE FIBROIDS

STUDY CENTRE: Institute of social obstetrics, Govt. Kasturba Gandhi Hospital, Madras Medical College, Chennai.

Patient may check (✓) these boxes

PARTICIPANT NAME AGE: I.D.NO.

I confirm that I have understood the purpose of the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason. Without my legal rights being affected. ☐

I understand that investigator, the institution, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I hereby consent to undergo complete physical examination and diagnostic tests including hematological, biochemical, radiological and urine examinations ☐

I hereby consent to participate in this study of PROSPECTIVE STUDY ON THE EFFECTIVENESS OF MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND THERAPY IN THE TREATMENT OF UTERINE FIBROIDS ☐

Signature of the Patient:……..Place……Date

……..

Address……

Signature of the Witness: ……..Place……Date……

Signature of the Investigator: …….Place……Date……

BHARAT SCA
Innovation at wo

22.11.2011

To
Dr.P.M.Gopinath,M.D.,D.G.O.,
FMMC FICS FICOG,M.B.A.,
Director of Social Obstetrics I/C
Institute Of Social Obstetrics
Govt.Kasturba Gandhi Hospital For Women & Children
Triplicane,
Chennai-600 005.

Respected Sir,

Sub: Request to send genuinely poor patients for HIFU

We are introducing the MRI Guided HIFU in our centre. In this regard I would like to extent my invitation to offer free services for a limited number of poor and needy patients from your esteemed hospital.

This procedure is much beneficial to the patients for the following reasons:

1. No radiation
2. Outpatient procedure
3. No surgery
4. No scars
5. No hospitalization
6. Painless
7. No expenditure to the poor and needy patients

I request you to pass on this benefit to the poor and needy patients.

Thanking you,

Yours Faithfully,

(Dr.R.Emmanuel,M.D.,R.D.)
Managing Director
9841049507

**INSTITUTIONAL ETHICS COMMITTEE**
**MADRAS MEDICAL COLLEGE, CHENNAI -3**

Telephone No : 044 25305301
Fax : 044 25363970

## CERTIFICATE OF APPROVAL

To
Dr. A. Devilakshmi
PG in MD OG
KGH / Madras Medical College, Chennai -3

Dear Dr. A. Devilakshmi

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Effectiveness of magnetic resonance guided high intensity focused ultrasound on fibroid ablation" No. 03012012.

The following members of Ethics Committee were present in the meeting held on 27.01.2012 conducted at Madras Medical College, Chennai -3.

| | | |
|---|---|---|
| 1. | Prof. S.K. Rajan. MD | -- Chairperson |
| 2 | Prof. Pregna B. Dolia MD<br>Vice Principal, Madras Medical College, Chennai -3<br>(Director , Institute of Biochemistry, MMC, Ch-3) | -- Member Secretary |
| 3. | Prof. B. Kalaiselvi. MD<br>Prof of Pharmacology ,MMC, Ch-3 | -- Member |
| 4. | Prof. Shruti Kamal MS<br>Prof of Surgery, Madras Medical College , Ch-3 | -- Member |
| 5. | Thiru. S. Govindsamy. BA BL | -- Lawyer |

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

# *PLAGIARISM REPORT*